THE NEWER KNOWLEDGE
OF NUTRITION

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THE NEWER KNOWLEDGE OF NUTRITION

THE USE OF FOOD FOR THE PRESERVATION OF VITALITY AND HEALTH

BY

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To

DR. C. EIJKMAN

Professor of Hygiene
in the University of Utrecht,
Who First Produced Experimentally
a Disease of Dietary Origin,

THIS BOOK IS DEDICATED

PREFACE

The science of nutrition has now reached a stage of development where it seems highly desirable that its history should be written, notwithstanding the fact that at present it is attracting the attention of a greater number of investigators than at any time in the past. There are distinct signs that discoveries of practical value in this branch of physiological chemistry will not be made so rapidly in the future as they have been during the past seven years for the reason that the relatively simple technic which has characterized the experimental work in this field gives no promise of bringing to light further spectacular results.

The experimental methods hitherto described can, when the necessary labor and money are expended upon them, perfect our understanding of the quantitative relations of the amino acid content of the individual proteins and mixtures of proteins which occur in natural foods of animal and vegetable origin. They can, furthermore, serve as an aid to the isolation in a state of purity of the several vitamins, although they are but poor and unwieldy substitutes for chemical tests, which, unfortunately, are still wanting. The tree of nutritional knowledge appears, however, to have grown to proportions which reveal the general outlines which it will always present, and further researches by the methods which have hitherto been so productive, can, it seems, only clothe it in attractive foliage and aid it in maturing the rich setting of fruit which has not yet ripened and fallen for the service of man, although a few windfalls which have been tasted reveal the keen enjoyment with which the human race will one day reap the full harvest.

In the preface to the third edition of The Science of Nutrition, Professor Graham Lusk said in 1917: "In another decade the development of scientific knowledge will probably permit the formulation of the subject from the standpoint of physical chemistry. It cannot now be so treated." It seems to the author that a few years must elapse, during which the structural changes in the protoplasm of the different tissues which result from specific faults in the diet are accurately described, before the methods of physical chemistry and the chemistry of colloidal substances

can be most effectively applied to the problems of physiology. Recent researches on the anatomic changes seen in beri-beri, rickets, scurvy and ophthalmia of dietary origin, represent the beginning of the task of preparing the field for the physical chemist. It is perhaps not too optimistic to hope that the next six years may see the fulfillment of Professor Lusk's prophecy.

It seems certain that a new era in nutrition investigations is at hand. Hitherto this branch of science has been the monopoly of the physiological chemist. He must now share his heritage with the histologist and the pathologist, and the three must work together. The chemist cannot progress far toward interpreting the nature of the changes which take place when the diet is faulty in any specific sense. He can interpret now, the exact nature of the dietary error which has produced in his experimental animal a pathological state, but with existing methods of analysis he cannot discover what part of the structures of the protoplasm have been injured. He can see loss of function but cannot explain its mechanism. He cannot tell what changes have taken place within the cells of special tissues as the result of his deliberate disturbance of their nutrition.

The science of pathology now suddenly has revealed to it an opportunity in a broad field of great practical importance, which it has never before enjoyed, viz.: an opportunity to investigate morbid anatomy and changes of function with a background of chemical explanation as to etiology.

In the vast literature which has grown up within a few years, relating to nutrition investigations, there is much that is confusing to one who would undertake to familiarize himself with it. Faulty technic, unwarranted deductions, premature conclusions, and conflicting data were inevitable in investigations involving so many variables and unknown factors. It seemed to the author that there is great need of a careful and critical interpretation of the existing data relating to nutrition, in order that the science may appear in its proper perspective. It was with this objective that the present volume was written. In order that the subject might be clarified it was necessary that elements of weakness in a considerable amount of experimental data should be pointed out.

The ultimate aim of scientific investigations is to give man control over the forces of Nature. The science of nutrition gives promise of making possible the realization of the optimal condition of physical well-being, with all that this implies for the mental achievement, freedom from physical defects including

tooth decay, and immunity to many of the ills which result from invasion of the tissues through breeches in the barriers of bodily defense, especially through decayed teeth and a debilitated alimentary tract.

The author has, during recent years, devoted much study to the dietary habits of peoples in different parts of the world with a view to correlating the results of animal experimentation with those of human experience in the use of different types of diets. The results of this study are presented in this volume. It is believed that these two lines of investigation, discussed as they are in their relation to each other, point unmistakably to a dietary regimen which will when adopted bring about marked improvement of the human race.

It is a privilege to acknowledge the services rendered by Dr. V. E. Levine, who carefully read the manuscript during its preparation and made many helpful suggestions for its improvement, and by Dr. P. G. Shipley, who also read the manuscript and assisted in the preparation of the chapter on rickets. Special appreciation is due Miss Nina Simmonds for her constant interest and criticism, and for assistance in the preparation of the bibliography and the index. Her familiarity with the extensive literature of nutrition and the critical sense with which she has examined it, contributed in no small degree to give the book such value as it may possess.

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CHAPTER I

THE BEGINNING OF A NEW ERA IN NUTRITION STUDIES

1. **The Method of Study of Nutrition Problems.**—Our knowledge of nutrition has progressed hand in hand with the development of the science of Chemistry. Chemical science has given us the clue to an understanding of the nature of the foodstuffs and the changes which take place in digestion, as well as an appreciation of some of the secrets of the metabolic processes which take place within the tissues of the body. Chemistry will continue as time goes on to aid in extending our knowledge of the finer processes of physiology. Nevertheless, it has been possible for a time to advance more rapidly in the study of nutrition, from the theoretical as well as from the practical standpoint, by a systematic feeding of simplified diets to animals, than by means of chemical studies. The results are interpreted on the observations as to the ability or inability of the animals to develop as the diets are modified. Progress has resulted in the past, and will continue in the future to come from the judicious division of labor between the study of food problems by chemical methods and by animal experimentation. In this brief exposition of the present situation respecting our knowledge of foods and nutrition it is desired to present to the reader an appreciation of the viewpoint of an investigator. It will be possible in this way to convey to him an appreciation of the line of reasoning by which the successive steps in the progress of the last few years have been attained. A brief historical account of the researches in this field will serve this purpose. It will, at the same time, illustrate the mental processes of the students engaged in bringing order into this field of scientific inquiry, where before there was no clear understanding.

2. **The Principal Components of Protoplasm.**—A plant structure or an animal body is an exceedingly complex system of

chemical substances, many of which are themselves individually as complex in their structure as the most complicated machine. The first step in the direction of reaching an understanding of the chemistry of the living tissues must involve the separation and study of the structural units of which they are composed. This was, indeed, the field of activity of many organic and biological chemists during the nineteenth century. The fats and the simpler substances into which they can be converted in the process of saponification were the subjects of exhaustive studies. The complex carbohydrates and the simpler sugars were discovered, and the manner in which they are related chemically was made clear. The most complex of the food substances, the proteins, were by far the most difficult to study by chemical means. Familiar examples of these are egg white, the casein of milk, and the principal components of meat. Certain proteins which occur in our plant and animal foodstuffs differ very greatly in their physical properties, but they are nevertheless very closely related chemically, since they can all be resolved into the same digestion products. These have been studied with marked success as to their behavior with the digestive juices produced in the pancreas or alimentary tract and with chemical reagents in the laboratory. In addition to these prominent components of plant and animal structures, a long list of relatively simple chemical substances have been discovered and isolated in a state of purity from vegetable and animal tissues. They have been investigated to determine their composition and special properties, and tests by means of which they can be recognized and identified and methods for their quantitative estimation in certain cases have been worked out.

Through a century of patient labor by many able men we came to an appreciation of the number and character of the simple structural units into which the tissues of an animal or a plant can be separated. Furthermore, certain of these simple bodies could be recognized as intermediate products in the course of the building up of more highly organized complexes; certain others were shown to be degradation products resulting from the physiological activity of the living tissues. Through these studies it became established that the body of an animal or the tissues of a plant consist essentially of proteins, carbohydrates, fats, and a series of related substances which are collectively known as lipins. The proteins are rich in the element nitrogen, the average content of this element being not far from 16 per cent. Several other prominent components of the living tissue contain

more or less of this element, so that this is not an essential characteristic. With these substances there are always associated in the living tissues more or less water and a number of inorganic elements in molecular or ionic form. A number of special kinds of each of the types of substances enumerated above became known, and their less obvious characteristics were described. Certain substances were found to be special products elaborated only by certain tissues and under definite conditions. These became regarded from the standpoint of nutrition as of subordinate interest. Examples of these are the alkaloids, quinin, strychnin, and cellulose. This last one serves as skeletal tissues for the plant but is not essential for the animal. In the same category belong the waste products of the life processes of the animal body, such as urea, uric acid and creatinin, most of which are not found in plant tissues.

Living structures on analysis, although always associated with numerous substances, the exact importance of which could not in many cases be determined, were found to consist essentially of proteins, carbohydrates, fats, mineral salts and water. These came to be regarded even as early as 1840 as the essential and never failing components of plant tissues, and were looked upon as the fundamental factors in the diet of animals.

3. **The Study of Foodstuffs by Chemical Methods.**—It became very early the principal activity of investigators in nutrition to discover and perfect methods for the analysis of foodstuffs, in order to determine the amounts of protein, carbohydrate, fat and ash contained in them. There were observed pronounced differences in the composition of the many substances which serve as food for man and animal. Meats, milk, eggs and a few seeds, such as the pea and bean, are very rich in protein. The cereal grains contain much less of this foodstuff, and the fruits, tubers and vegetables, especially in the fresh condition, contain very little. Equally great variations are observable in the water content of foods, and in their yields of fats and carbohydrates. One of the great epochs in the development of the science of nutrition is that in which Atwater and his associates in America, and Voit in Germany, examined and tabulated in classified form the chemical composition of an extensive list of human foods (1). Following this, Agricultural Experiment Stations accumulated similar data concerning substances used for feeding animals. Previous to 1900 the idea that there was any marked variation in the quality of proteins

from different sources did not become generally appreciated.

It seems remarkable, in the light of the revelations in the field of nutrition during the last few years, that close students of nutrition accepted for so long, and without experimental proof, the belief that the results of a chemical analysis revealed the dietary values of foodstuffs.

4. Advances in Our Knowledge of Digestion.—The processes of digestion of food are so remarkable that they have been made the subject of extensive study by many of the ablest students of physiology and biochemistry. The chemistry of the fats and carbohydrates is somewhat simpler than that of the proteins, and their structure and transformations came to be earlier understood. It was not until the close of the nineteenth century that the nature and extent of protein digestion became fully appreciated. Soon after 1900 the researches of Kossel and of Fischer revealed the great variation in the composition of proteins from different sources (2). This discovery introduced into nutrition studies the idea of quality of protein in addition to quantity. A statement of the quantity of protein had hitherto seemed satisfactory to students of nutrition. Most proteins were found to be resolvable into seventeen or eighteen simple digestion products called amino-acids, and it was observed that the proportions in which these were present in the protein molecule varied greatly in the proteins from different sources. All or nearly all of these digestion products appear to be indispensable components of an adequate diet. The extensive and valuable researches of Osborne have shown that all natural foods contain several proteins (3). Although there are individual proteins, such as gelatin and zein (from maize), which are entirely lacking in one or more of the essential digestion products, every natural food appears to contain more or less of each of them. The protein mixture, which is found in any natural food, such as the grains, tubers, meats, etc., may be regarded as biologically complete, but their biological values differ greatly, depending on the yield of the several amino-acids obtained from them.

This appreciation of the differences in biological values of proteins from different sources represented an awakening from a state of tranquillity among physiologists, who had come to believe, about the year nineteen hundred, that chemistry had revealed all the more important facts relating to foods and nutrition. As we look back now upon the recorded observations which had been made from time to time for centuries, especially by

those whose viewpoint was essentially that of the pathologist, it is difficult to see how all the able students of nutrition during the nineteenth century should have so completely ignored their findings which pointed to a close relation between the diet and disease.

5. **Students of Nutrition Failed to Profit by Human Experience.**—In several parts of the world restricted diets of a monotonous character have for centuries produced diseases in man. The only one of these which was at all common in the Western hemisphere was scurvy. This disease caused much suffering among sailors in the days of the long voyages before the advent of steam navigation. It was well understood from the early part of the eighteenth century that scurvy was the result of the consumption of a faulty diet composed usually of biscuits and salt meats. It was also known that prompt recovery resulted from the consumption of liberal amounts of fresh fruits and vegetables. Decades passed without any systematic attempt being made to determine the cause of the peculiar value of this class of foods.

Pellagra has been a scourge among the poorest peasants in some parts of Italy and France for centuries, and its etiology has been referred by many to the poor quality of the simple and monotonous diet. This disease was not observed in America until after 1900. After that time it increased rapidly up to 1917, especially in the Southern States.

Beri-beri is a disease common among the poorest classes of the Orient, who limit their food supply principally to polished rice and fish. It is remarkable that not until the year 1897 was the first fertile suggestion made as to the nature of the dietary fault which was responsible for the development of this disease. This observation was made by the Dutch physician, Eijkman.

Man has been sufficiently industrious in most parts of the world to secure for himself a varied diet, which he derives from the cereal grains and legumes, fruits, roots, tubers, meats and certain edible leaves. Beginning with the dawn of the era of his most rapid advance toward achievement, he has in many parts of the world been the possessor and protector of flocks and herds, which provided him with clothing and a constant supply of meat and milk. The importance of this last item in his food supply we have but recently come to appreciate. The famous chemist, Van Helmont, called milk "brute's food," and thought it advis-

able to substitute for it bread boiled in beer and honey. Baron Liebig likewise thought of preparing a substitute for milk in his "Food for Infants." In later chapters of this book it will be made clear how tragic it is for the health of an infant to attempt to replace the most important single human food by some mixture made up on the basis of chemical composition in imitation of human milk. It is with a view to establishing an appreciation of the great differences in the nutritive value of foods the composition of which is such as to make them appear alike from the results of chemical analysis, that the present account of the progress attained by the investigations of recent years was prepared.

6. An Experiment which Stimulated Investigations along New Lines.—In 1906 an experiment was begun at the Wisconsin Experiment Station which had a far-reaching effect on the minds of students of nutrition. It was planned by S. M. Babcock, and was carried out by Hart and Humphrey, with the later co-operation of Steenbock and the author. In this experiment the object was to determine whether rations for cattle so made up as to be alike insofar as could be determined by chemical analysis, but derived each from a single plant, would prove to be of equal nutritive value for growth and the maintenance of vigor (4).

The ration employed for one group of animals was derived solely from the wheat plant, and consisted of wheat straw, wheat gluten and the entire wheat grain. The ration of a second group consisted of the entire corn plant, which included the kernel, stalk, and the leaf, together with a portion of corn gluten, a by-product of the cornstarch industry. The third group obtained their ration solely from the oat plant, being fed entirely on rolled oats and oat straw and leaf. There was a fourth group, which it was supposed would serve as controls, that was fed a ration having the same chemical composition, but derived from about equal portions of wheat, corn and oat products.

The animals employed were young heifer calves weighing about 350 pounds, and were as nearly comparable in size and vigor as could be secured. They were restricted absolutely to the experimental ration. They were given all the salt (NaCl) they cared to eat, were well cared for, and were allowed to exercise in an open lot free from vegetation. Their behavior during growth and during the performance of the functions of reproduction were extremely interesting. All groups ate practically the same amounts of feed and digestion tests showed that there were no differences in the digestibility of the three rations.

7. **The Corn Plant a Better Ration for Cattle Than the Wheat or Oat Plants.**—It was not until the animals had been confined to the experimental rations for a year or more that differentiation in their appearance was easily observable. The corn-fed group was sleek and fine, and evidently in an excellent state of nutrition. In marked contrast stood the wheat-fed group. These animals were rough coated and gaunt in appearance, and small of girth as compared with those fed the corn-plant ration. The weights of the two groups did not differ in a significant degree. The groups fed the oat-plant ration and the mixture of the three plants, leaf and seed, stood intermediate between the lots just described. The assumption that the animals receiving the mixture of products would fare better than the others, and thus serve as the standard group for controls, did not prove correct. The corn-fed animals were at all times in a better state of nutrition than were those receiving the greater variety of food materials.

8. **Vitality of Young Depends on the Character of the Diet of the Pregnant Mother.**—The reproduction records of these animals are of special interest. The corn-fed heifers invariably carried their young to full term. The young showed remarkable vigor, and were normal in size and able to stand and suck within an hour after birth, as is the rule with vigorous calves. All lived and developed in a normal manner. The young of the wheat-fed mothers were the reverse in all respects. They were born three to four weeks too soon, and were small, weighing on an average 46 pounds, whereas the young of the corn-fed animals weighed 73 to 75 pounds each. The latter weight is normal for new-born calves. The young of the wheat-fed mothers were either dead when born or died within a few hours. The young of the mothers which had grown up on the oat-plant ration were almost as large as those from the corn-fed mothers, the average weight being 71 pounds. All of the cows in this group produced their young about two weeks too soon. One of the four was born dead, two were very weak and died within a day or two after birth. The fourth was weak but with care it was kept alive. The young of the cows which were fed the mixture of the three-plant products were weak in most cases. One was born dead and one lived but six days. The mothers were continued on the experimental rations and the following year they repeated in all essential details the reproduction records observed in the first gestation periods.

9. **Milk Production as an Index to Vitality.**—Records were

kept of the milk production during the first thirty days of the first lactation period. The average production per day per each individual of the corn-fed lot was 24.03 pounds; for the wheat-fed animals 8.04, and for the oat-fed animals 19.38 pounds. Those fed the mixture of the three plants produced an average of 19.82 pounds of milk per cow per day during the first thirty days. In the second lactation period the average figures for milk production were 28.0, 16.1, 30.1 and 21.3 pounds, respectively, per day during the first thirty days.

Through autopsy and analysis of the tissues of the young, and analysis of the feeds and excreta of the animals of the several groups, an elaborate attempt was made to solve the problem of the cause of the marked differentiation of the animals fed these restricted diets. Interesting data were secured which showed marked differences in the character of the fat in the milk of the cows of the different lots. The observation was made that the urine of the wheat-fed animals was invariably distinctly acid in reaction, whereas that of the other lots was alkaline or neutral. It was not possible by any means known to biological chemistry to work out a reason as to the cause of the pronounced differences in the physiological well-being of the different lots of cows.

10. **A New Method of Investigation Was Necessary if Further Progress Was to Be Made.**—This experiment confirmed the author's conviction that the only way in which the problems of nutrition could ever be solved was to work out the problem of the successful feeding of the most simplified diets possible. If this were accomplished it would be possible to proceed from the simplest diet to the complex diets employed in practical nutrition. It would also be possible to ascertain the nature of the dietary faults in each of the natural foods, singly, the seed alone and the leaf alone, before attempting to interpret the cause of malnutrition in animals fed the more complex mixtures.

Several investigators had already made efforts to nourish young laboratory animals on mixtures of purified protein, starch, sugar, fats and mineral salts, but in all cases without success. Steinitz (5), Leipziger (6), Zadik (7), Ehrlich (8), Socin (9), Hall (10), Falta and Nöggerath (11), Jacob (12), Marcuse (13), Henrique and Hansen (14), and Willcock and Hopkins (15), had all employed such food mixtures. In all these trials directed toward the nutrition of animals with food mixtures which contained everything considered in the ordinary food analysis, the

animals lost weight steadily from the beginning of the experiments. They died unless the diet was changed. It was impossible at the time to explain the reason for their failure.

11. **Nutrition Studies Must Be Conducted with Small Animals.**—Studies of this character must of necessity be carried out with small laboratory animals, because it is difficult and laborious to prepare the purified foodstuffs in sufficient amounts for the conduct of feeding experiments. It is, however, highly desirable to shorten the length of such experiments as far as possible by the employment of short-lived omnivorous animals which grow rapidly and which quickly reach maturity. In this way it is possible to accumulate data sufficiently fast to make progress reasonably satisfactory. The domestic rat serves this purpose admirably. It has a gestation period of but 21 days and, under normal conditions, the young are ready to wean at the age of 25 days. The female, when well nourished, usually produces her first litter at the age of 90 days, and will, if properly handled, have five or more litters by the time she reaches an age of fourteen months, which age ordinarily marks the end of her period of fertility. The extreme span of life of the well-fed rat is about thirty-six months. By using such an animal it is possible to accomplish within a relatively short time the accumulation of data regarding growth and reproduction which it would take years to secure with domestic animals of large size, long period of gestation and long span of life. With the latter the expense would be prohibitive. In 1907 the author took up the study of the cause of the failure of animals to grow on mixtures of purified foodstuffs and employed the domestic rat as the experimental animal.

12. **The Problem of the Importance of Organic Forms of Phosphorus.**—As can be seen by the titles of several of the papers cited in connection with the feeding of isolated and purified food substances, one of the earliest explanations which occurred to investigators as the possible cause for the failures was the probable need of the animal for phosphorus in certain organic combinations. Some of the experiments were interpreted as supporting the view that proteins containing phosphorus as a part of the molecule were better utilized for growth than were phosphorus-free proteins. Between 1895 and 1910 there was a widespread belief among students of this subject that the presence of organically bound phosphorus might be a factor of great importance in nutrition. It is easy to appreciate how this idea

gained credence. Casein, the principal protein of milk, is a phosphorus-containing protein, and the yolk of egg is very rich in both the phosphorized protein, vitellin, and in phosphorized fats. Milk and the egg yolk are peculiarly constituted for the rôle they play in reproduction and the nutrition of the young during the earliest period of post-natal life when growth is most rapid. It seems significant that in these two substances organically bound phosphorus is very abundant, whereas it is abundant nowhere else among our natural foods. It has never been conclusively shown up to the present time that a protein occurs in plant tissues which contains the element phosphorus as a part of its molecule. Other organic phosphorus compounds (lecithins, nucleic acids) do exist in plant tissues but never in great abundance.

Among the experiments cited above in which animals were confined to diets of purified proteins, carbohydrates, fats and mineral salts, those of Hall, Steinitz, Leipziger, Zadik and Ehrlich were directed towards ascertaining the importance of phosphorus in organic as contrasted with inorganic combinations. Other investigators working along the same lines were Kornauth (16), Gottstein (17), Ehrstrom (18), Hirschler and Terray (19), Gilbert and Posternak (20), Tunnicliffe (21), LeClerc and Cook (22), Koch (23), Hart, McCollum and Fuller (24), and Forbes (25). The evidence either seemed definitely to support the view that organic phosphorus compounds were essential in the diet or else it failed to establish the fact that they were dispensable.

13. **Inorganic Phosphates Suffice for All Nutritive Needs of an Animal.**—In 1909 McCollum (26) introduced a new feature into experiments of this type by seeking to increase the variety of foodstuffs in the diet as far as possible, with the hope of obtaining success where others had failed to secure satisfactory nutrition in animals. In the series of experiments referred to the one condition which was required of every organic component of the ration was that it should be free from phosphorus in any form. This condition was practically met. The only source of phosphorus in the diet was finely ground tricalcium phosphate, a natural mineral.

14. **A Mistaken Conclusion Which Stimulated Research in a New Direction.**—This paper is deserving of special notice because it reported the first successful growth experiments with a food supply which was at that time considered as essentially

a mixture of purified foodstuffs, every one of which could be named. It seemed to demonstrate that the view, which had long held sway, that the only substances necessary in the diet are proteins, carbohydrates, fats and certain mineral salts, was indeed well founded. It appeared to prove that the cause of the failure of the earlier experiments of this type was due to the lack of palatability of the food, which led to failure of the animals to ingest sufficient quantities of food. This was one of the conclusions of the author, but it has since become apparent that this viewpoint was a mistaken one.

The proteins employed were edestin from the hemp seed and zein from maize. Corn starch, wheat starch, milk sugar, glucose, cane sugar, butter fat, bacon fat, and cholesterol, a substance found in most body tissues and having physical properties similar to fats, together with the ash constituents, made up the food supply. No effort was made to feed a constant mixture. On the contrary, the diet was changed from day to day as far as possible in order to prevent the dreaded loss of appetite. On this food supply several young rats gained in weight, one somewhat more than doubling its weight in fifty-six days. These results were interpreted as meaning that growth had actually been induced by a mixture of purified food substances, where all previous attempts had failed. The only difference between the experimental diet used in this study and those of the earlier investigators appeared to be in the palatability factor. Important deductions were drawn from these results concerning certain synthetic reactions which the body tissues could accomplish. Five years later it became apparent that the cause of the growth of this group of animals lay in the chance inclusion in the diet of milk sugar, which was not as pure as it was supposed to be, and to the inclusion of butter fat. Each of these we now know furnished a substance indispensable for either growth or maintenance. But a surprisingly small amount of each of these is necessary in order to induce the maintenance and the growth secured in these experiments.

15. A New Opportunity to Compare the Nutritive Values of Individual Proteins.—On the publication of the paper in which these experimental results were described in 1909, it appeared to be established that the long accepted views concerning what the diet must contain in order to be adequate, were correct, and that the chemical methods for the analysis of foods actually afforded data from which the nutritive properties of a diet could

be appraised. The data also seemed effectually to dispose of the disputed question concerning the relative merits of phosphorized as compared with phosphorus-free proteins, and indeed, could be interpreted only to mean that the animal body is capable of synthesizing from salts of inorganic phosphoric acid, all the complex phosphorus-containing organic substances which are so important as components of living matter.

These ideas being accepted as proven facts, it seemed that the next great advance in the field of nutrition investigations was in the field of study of the relative values of the numerous proteins of the plant and animal tissues, which organic chemists had been recently studying by improved methods, and which they showed to be very differently constituted when derived from different sources. The chemical methods were not entirely satisfactory for the analysis of these complex bodies. Even in the hands of the most skilled chemists, among whom Kossel, Fischer, and Aberhalden in Germany and Osborne in America were the most noted, only a little more than half of the protein molecule could be accounted for in the form of identifiable products of digestion, the amino-acids. Obviously such analyses, although representing a marked advance in chemical science, were too incomplete to permit of using them as a basis of judgment as to the nutritive values of individual proteins. The way now seemed open, however, for the quantitative comparison of individual proteins, carefully isolated and purified, by feeding a single protein as the sole source of this dietary factor, and with a diet which was otherwise complete and satisfactory. A series of such experiments in which proteins from various sources were employed, should reveal differences in their values for transformation into body proteins during growth. The experimental studies of McCollum, just discussed, seemed to make such investigations possible. In 1909 Osborne and Mendel undertook to carry out such a series of researches on purified proteins. Osborne had for many years made a thorough study of the number and nature of the proteins in various cereals, legume seeds, nuts, oil seeds and of certain animal tissue proteins, and possessed the knowledge, skill and equipment for their preparation on a large scale.

16. Two Vitamins Were Present in Foods Supposed to Be Purified.—Unfortunately, for the progress of this branch of physiological chemistry, the diet which McCollum had employed successfully for the promotion of growth in young rats was something more than it appeared to be. It was not actually a

simple mixture of proteins, several carbohydrates, fats and inorganic salts, but contained as impurities, two nutritive principles which were unsuspected. One of these was in the milk sugar, although this was believed, on the basis of careful tests, to be highly purified lactose; the other was an uncharacterized substance which the butter fat contained. The failure of all investigators in this field to appreciate this led to confusion for several years. The further history of investigations which cleared up this problem will be given in the following chapter.

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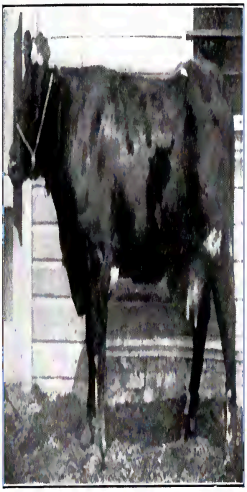

Fig. 1.—Photograph of a cow which grew up on a ration derived solely from the corn plant. The seed, straw and leaf of the plant were all included in the food mixture. Her nutrition was excellent, as shown by her appearance, the vigor of her offspring and her ability to produce an abundance of milk. Figure 2 shows a photograph of her calf, taken soon after it was born. Rations consisting of the entire plant may be highly satisfactory. The seed of the plant is never in itself a complete food.

FIG. 2.—Photograph of calf produced by a mother whose ration had been long derived from the corn plant as the sole source of nutriment. It was vigorous and developed normally. The entire wheat plant, seed, leaf and stem make a diet which can support growth, but not good nutrition. The corn kernel alone does not induce growth.

Fig. 4.—Calf produced by cow shown in Figure 3. It was born prematurely, weighed but little more than half as much as calves normally do at birth, and was dead when born. The importance of the source of the food supply, both for the nutrition of mother and the unborn young, is strikingly illustrated by these animals. (Figures 1 to 4 are from Research Bulletin 17 of the Wisconsin Experiment Station.)

CHAPTER II

A BIOLOGICAL METHOD FOR THE ANALYSIS OF A FOODSTUFF

17. **McCollum's Experiments Not Verified by Osborne and Mendel.**—It was pointed out in the preceding chapter that repeated failures characterized experimental studies in which animals were confined to diets containing only the well established food principles. These failures had practically established the belief that this line of study was unprofitable, because all animals, for some unknown reason, died when confined to such a regimen. The apparently conclusive results of McCollum with such mixtures aroused hope that a new and valuable body of data could be secured which would reveal the sources of the valuable and less valuable proteins among our natural foods.

In 1909 Osborne and Mendel took up this line of investigation and proceeded to feed individual proteins with a diet which was otherwise composed of purified starch, lard and mineral salts. At the outset of their studies they accepted the evidence which McCollum had presented that this could be successfully done and planned to interpret on the basis of the capacity of young rats to grow on a constant diet, varied in successive experiments only with respect to its protein, the relative merits of such proteins as tissue builders. They did not, however, actually duplicate the experimental conditions of McCollum, but adopted a diet which they regarded as having essentially the same properties. This consisted of purified protein, such as casein of milk, starch, lard and a salt mixture. They met with complete failure in these attempts to nourish their animals with such a diet. They tried a salt mixture recommended by Röhmann (1) with which he had met with success with a diet consisting in great measure of purified food substances, and also the salt mixture described by McCollum. In all cases, however, their animals declined steadily from the time they were confined to such diets. They proceeded a step farther and established the fact that the failure of the animals was not due to lack of appetite,

since the food intake was found to be sufficient to promote growth provided the composition of the food had been satisfactory. At that time no one was able to see any important difference between the quality of a purified protein, three carbohydrates, *one being milk sugar*, two kinds of fats, *one being butter fat*, and a salt mixture, as compared with a simple mixture of protein, starch, lard and salts.

18. **Osborne and Mendel Prepare "Protein-Free Milk."**—Following their failure to nourish animals satisfactorily on a diet of isolated and purified foodstuffs, Osborne and Mendel (2) adopted what they apparently regarded as essentially the equivalent of a mixture of purified food-stuffs. The basis of their new diet was 28 per cent of "protein-free milk," a product made by removing as completely as possible the fat, casein and lactalbumen from milk, and evaporating the resulting whey to dryness. The residue was a yellow solid, easily ground to a powder, consisting for the most part of milk sugar and the mineral salts originally present in the milk. In fact, no other components of the product could be named. "Protein-free milk" was found to contain about 0.7 per cent of nitrogen, but the form in which it was present could not be ascertained.

They prepared diets, using 28 per cent of this "protein-free milk," the remainder of which consisted of starch, lard, agar-agar, and the protein which they desired to study. This combination had certain properties which could not be accurately defined, but which made it far superior to any of the simple mixtures used by others. With these diets they were able *with certain proteins* to secure in rats normal growth to the full adult size. The results, judging from the widespread comments on these experiments, were regarded by many as the final triumph in this type of experimental work.

Since Osborne and Mendel considered their diet containing "protein-free milk" as suitable for the purpose which they had in view, the comparison of the relative values of various isolated proteins, they apparently abandoned further efforts to solve the problem of what was lacking in their former diets of purified food-stuffs. They did, however, prepare an "artificial protein-free milk" from what they regarded as pure milk sugar and a mixture of mineral salts made up from reagent bottles,—an attempt being made to imitate exactly the composition of the "natural protein-free milk." With this mixture in place of the natural product they secured excellent growth records over

periods covering two months or a little longer (3). They made a special effort to secure lactose and salts of a high degree of purity for certain of their experiments in which "artificial protein-free milk" was used. This preparation gave negative results in most cases, and in all the amount of growth was decidedly less than when materials of ordinary purity were used. They carried their investigations in this direction no further than to make the addition of traces of iodin, manganese, fluorin and aluminum. These additions, the "impurities" suspected in their reagents of poorer quality, actually improved the diet, making it capable of inducing better and more continuous growth, which, however, ceased before growth was completed. Osborne and Mendel were for a time inclined to accept the view that the peculiar virtue of their natural "protein-free milk" lay in the nice adjustment of the inorganic elements and radicals it contained.

19. **Students of Nutrition Had Ignored the Observations of Pathologists on Deficiency Diseases.**—With this understanding of the experience and views of the various investigators of the subject of nutrition, it is of interest to look back from our present position and point out the problems waiting to be solved.

There had been in the literature of pathology for many years abundant evidences from human experience that a diet may have an appropriate chemical composition and yet be unsatisfactory for the nutrition of man. These observations did not secure from students of nutrition the attention they merited. It had been known for centuries that certain diets of stale foods produced outbreaks of scurvy among sailors, soldiers, prisoners and others, and that fresh vegetables and fruits would promptly relieve the trouble if they were taken in the early stages of the disease. Nobody had, however, even in the first decade of the twentieth century, made an effort on a comprehensive plan to discover what it was in certain foods which caused them to be incomplete and to induce disease, and what it was in certain other foods which made them of specific therapeutic value.

Beri-beri, a peripheral neuritis resulting in paralysis, had been known from remote times. In 1884 it was demonstrated beyond doubt by the Japanese Navy that it was due to faulty diet. Under the direction of Admiral Takaki a ship made a cruise of eight months, during which time the incidence of beri-beri among the sailors was carefully noted. Another ship was then manned and sent on a second cruise over the same course, but with an improved dietary furnished the men. The effects were so strik-

ing that the diet of the army and navy was remodelled and improved, with the result that thereafter the disease practically disappeared. In 1897 Eijkman, a Dutch physician, sought to test the question whether there was any relation between the consumption of polished rice and the incidence of beri-beri. He found that pigeons or chickens that were restricted to a diet of milled rice developed in two to four weeks a condition of paralysis strikingly suggestive of beri-beri in man. He established the relation between milled rice and the disease, and showed that there was something in the bran layer which protected against it. Although several pathologists had repeated and confirmed this observation, it did not influence students of nutrition until after Funk, a Polish chemist, called attention to this work in 1910, when he designated the term "vitamine" to indicate a group of indispensable nutritive complexes (4).

20. **Funk Popularizes the Deficiency Diseases.**—To Funk is due the credit of bringing to the attention of all the view that there are certain diseases which result from faulty diet, the fault consisting in a lack, relative or absolute, of one or another of several substances, each of which when present in the diet protects against a specific type of breakdown of the tissues. Beri-beri, scurvy, pellagra and rickets were all attributed by him to lack of "vitamines" in the diet. Actually he had experimental evidence of the existence of only one of these specific "deficiency" diseases, beri-beri or polyneuritis, as it is called when produced experimentally in animals. This was the only one of the syndromes enumerated which had been studied experimentally in a manner that could be regarded as affording a basis for judgment as to their etiology.

Human experience had, however, been practically as definite as animal experimentation in demonstrating that scurvy could be cured with certain fresh foods, but not by the same foods in a stale condition. As will be pointed out later, however, there was much difference of opinion as to the cause of scurvy. The vitamins made a great impression on the public mind and justly so. There is nothing more spectacular than the restoration of a pigeon which has been brought to a condition of helplessness by a diet of polished rice. Within a few hours of death it can be brought back to an apparently normal condition by the administration of but an insignificant amount of properly prepared substance.

Funk had no clear conception of the importance of the several

factors which go to make up an adequate diet, for in 1910 he knew how to produce but one deficiency disease, polyneuritis or beri-beri. This was effected in the same manner that Eijkman had done it in 1897, by restricting animals to polished rice as their sole food supply. These observations in pathology failed at that time to impress the students of normal nutrition. Rice is now known to be faulty with respect to four dietary factors for the rat, and with respect to five factors for man.

21. McCollum Was Led by Osborne and Mendel's Results to Study Further the Purified Food Mixture.—It has been stated already that Osborne and Mendel (5) reported their failure to induce growth in young rats on a diet composed of purified casein, starch, lard and the inorganic salt mixtures employed by Röhmann and by McCollum, and it was evident from their records of food intake that sufficient food had been consumed to promote growth if the quality was satisfactory.

No explanation was apparent for their failure, for the diet of McCollum, with which successful growth had been reported, consisted of two pure proteins, several carbohydrates, including milk sugar, two fats, including butter fat, and a salt mixture (see p. 11). It had been supposed that the success observed with this food mixture was due to adequate food consumption. An effort was at once begun by McCollum to discover wherein lay the lack of harmony in these observations. As the situation stood, his work was discredited, and he felt that many would be inclined to regard his reported data as falsified. It was now imperative that he should satisfactorily explain why others had failed to confirm his results.

Returning, therefore, to this field of study, he found his results irregular and confusing. Employing a diet consisting of casein, dextrinized starch, *milk sugar*, and salts, he and Miss Davis tried the addition of a series of different kinds of fats, to see if any special virtue could be found in any of these, and in 1912-13, found that young rats restricted to such a diet could grow well when butter fat or egg yolk fats were incorporated in this food, but that olive oil or lard did not under these conditions induce any growth. These results were not described until June, 1913. They interpreted these results to mean that there was in certain fats a dietary essential which had not hitherto been recognized.

22. Investigations on the Synthesis of Complex Lipins by the Animal Body.—McCollum and Davis appreciated the fact that the animal body is capable of producing synthetically the

complex lipins, or fat-like substances such as lecithin, which in addition to glycerol and fatty acids contains phosphoric acid and a nitrogenous base called cholin. McCollum, Halpin and Drescher (6) had shown that young hens could grow for a considerable time on a diet free from this class of substances, and while confined to it, could produce many eggs in which were contained much more of the complex lipins than the bodies of the hens could furnish, they remaining in good health at the end of the experiment. Butter fat is free from lecithin and related substances, so their data led McCollum and Davis to the conclusion that the stimulating effect of butter fat on growth could not be attributed to any known lipin.

In 1912, Osborne and Mendel (7) published a paper describing successful nutrition over a considerable period of time with diets which contained no fats and but traces of substances soluble in fat solvents such as ether. This paper tended greatly to confuse the entire subject. They fed a diet consisting of purified protein, cane sugar, starch, and "protein-free milk," and in some of their experiments with similar diets "artificial protein-free milk" was used instead of the natural product. The artificial product was composed of milk sugar and a salt mixture from reagent bottles. It was made in close imitation of the mineral content which analysis showed to be present in the natural product. These diets, which contained no fats, were capable of inducing normal growth for a period of sixty days.

Commenting on these results Osborne and Mendel stated: "Employing the methods which were adopted in our earlier feeding experiments with isolated food substances, we have succeeded in inducing a normal rate of growth in white rats with dietaries devoid of fat throughout almost the entire period during which growth ordinarily continues." They stated that "McCollum has demonstrated that the phosphorus needed by an animal for phosphatid formation can be drawn from inorganic phosphates, and that phosphatids can be synthesized anew in the animal body. Röhmann asserts the possibility of lecithin synthesis in mice which were maintained into the second generation on lecithin-free food. Our own experiments point in the same direction with regard to the lipoids in general, and they give positive evidence of the dispensableness of true fats for growth."

23. McCollum and Davis Discover the Unique Dietary Properties of Butter Fat as Contrasted with Vegetable Fats and Body Fats.—When this paper appeared McCollum had already accumulated experimental data which led him to believe

that there were very great differences in the nutritional value of fats from several sources. With diets composed of protein, starch, milk sugar, salts, and fats, it had been found that prolonged growth was secured when butter fat was added. This had been dissolved in ether and passed through filter paper in order to make certain that no traces of any ingredients of the milk except the fats and substances having the same solubilities were present. Egg yolk fats behaved like the purified butter fat, whereas little growth and early failure resulted when olive oil or lard formed the only fats in the diet. Owing to an epidemic which destroyed the rat colony a year elapsed before a fairly satisfactory demonstration of this fact could be secured, the records of which seemed safe for publication. In June, 1913, McCollum and Davis (8) recorded their findings that carefully purified butter fat, all of which was soluble in fat solvents, and likewise egg yolk fat, contained something which greatly promoted growth, and that lard and olive oil did not possess this property.

24. **Osborne and Mendel's Observations on Butter.**—Osborne and Mendel had discovered by this time the error of their conclusion that growth and well-being could be secured in animals restricted to a diet free from fats and containing "but an insignificant trace of ether extract." The month following the appearance of the paper by McCollum and Davis demonstrating the peculiar value of certain animal fats as contrasted with other animal fats and with vegetable fats (8), Osborne and Mendel published a paper on "The Relation of Growth to the Chemical Constituents of the Diet" (3). They described in this paper the preliminary period of growth they secured with their diet of purified protein, starch, sugar, and "protein-free milk." This short period of growth, which rarely extended beyond sixty days, was followed by decline. The decline, they found, could be checked by the addition of 16.4 per cent of *butter*. Animals which received the butter from the beginning of the experiment grew uninterruptedly to maturity or nearly so. In their paper on nutrition with fat-free food-stuffs they had, curiously enough, interrupted their experiments at the end of sixty days or thereabouts from the time when the animals were restricted to the "protein-free milk" and "artificial protein-free milk" mixtures, and yet they described these records as successful growth "through almost the entire period during which growth ordinarily continues."

It was not possible to draw any conclusions from the data

presented in their paper now under discussion as to whether the unknown food complex present in *butter* was in the fat fraction or in the non-fat fraction of the latter. Butter contains about 15 per cent of milk substance other than fat. This portion consists, among other things, of water, protein, cells from the mammary gland, leucocytes, and bacteria, and it was impossible to decide without further evidence whether it was in some of these or in the fat itself that the substance occurred which exerted such remarkable effects on the growth of animals. Hopkins (9) had just reported that rats restricted to diets of purified foodstuffs steadily declined, whereas similar ones which were confined to the same diets, but in addition received 1 to 3 c.c. per day of fresh milk were able to grow. Even after decline had set in on the basal diet it could be checked by this small quantity of milk, which in no instance exceeded about 4 per cent of the dry weight of the diet.

CHART I

Journal of Biol. Chem., 1913, xv, 167

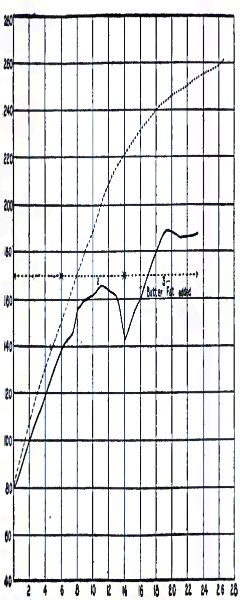

Chart 1 shows one of the original growth curves published by McCollum and Davis, which led them to the discovery of the

special growth-promoting properties of butter fat as contrasted with vegetable fats and certain animal fats.

CHART I (*Rat 141*, male) shows the record of a rat which grew continuously although slightly under normal rate during eighty days on a ration of relatively pure food substances. There was at this time a complete suspension of growth and a rapid decline in body weight. The addition of 10 per cent of ether-soluble butter fat to the diet led to a prompt resumption of growth during the following thirty-five days, when the rat gained 50 grams.

The rations employed were as follows:

PERIOD I	*per cent*	PERIOD II	*per cent*	PERIOD III
Salt mixture	6	Salt mixture	5	Same as II with butter fat replacing part of dextrin.
Casein	12	Casein	12	
Lard	20	Lactose	20	
Lactose	15	Dextrin	61	
Starch	42	Agar-agar	2	
Agar-agar	5			

The salt mixture employed consisted of:

	grams		*grams*
Sodium chlorid	0.61	Calcium lactate	11.38
Dipotassium phosphate	17.00	Magnesium citrate (10.2% Mg)	23.42
Monocalcium phosphate	1.63	Ferric citrate	1.00

The lactose in the diet was not entirely pure, and contained enough of the water-soluble B to support growth.

25. **Osborne and Mendel's Studies on Butter Fat and Other Fats.**—Five months later Osborne and Mendel (10) described experiments entirely analogous to those of McCollum and Davis, in which their animals were confined to purified protein, starch, "protein-free milk," lard and *butter fat.*

Although the final evidence which Osborne and Mendel offered as proof of the unsuspected value of butter fat in nutrition was of the same kind as had been presented five months earlier by McCollum and Davis, in which *butter fat* and *egg yolk fat* were shown to be similar, and superior to lard or olive oil, their paper attempted to minimize the importance of the work of McCollum and Davis. They stated that "In none of their (McCollum and Davis) published records was the recovery so rapid as in most of ours, nor was the rate or extent of growth, after reaching the previous maximum weight, any greater than on the butter fat-free diet earlier supplied." Further, "although the data furnished by McCollum and Davis strongly indicate that butter fat has a marked influence on growth, they by no means prove that butter

fat contains something essential for the metabolism of growth apart from that of maintenance."

It is now clear that the reason for the better growth of Osborne and Mendel's animals when butter fat was added to the diet was due to the fact that their "protein-free milk" contained an abundance of a second dietary factor, the anti-neuritic substance which prevents beri-beri, whereas the diets of McCollum and Davis contained decidedly less of this substance which was present as an impurity in the supposedly pure milk sugar which their diet contained. It seems certain that there is no substance essential for maintenance, apart from growth, as the last quoted sentence suggests. This idea has been in the minds of several investigators, but the evidence that normal maintenance can be secured on any diet lacking in a complex necessary for growth is very slender indeed. This point will be discussed in Chapter III.

Early in 1914 Osborne and Mendel (11) confirmed the observation of McCollum and Davis that egg yolk fats and cod liver oil had the same effect on growth that butter fat exerted, and that lard did not stimulate growth as did egg and milk fats. They investigated almond oil and found it to resemble olive oil in the respect that it did not promote growth.

26. Stepp's Experiments on the Indispensability of Certain Lipins in Nutrition.—The results of these investigations recalled the fact that as early as 1909 Stepp (12) had described experiments in which he had found that bread prepared with milk was capable of maintaining adult white mice without loss of weight for an indefinite period. When the same bread was extracted with alcohol-ether, the animals restricted to it rapidly declined. Replacement of the extracted material failed to restore the dietary properties of the original bread. In later experiments Stepp showed that the addition of the salts which were extracted with the lipoids did not prevent the rapid decline of the animals. *Butter additions did not prevent decline*, but the addition to the extracted bread, of lipin extracts of egg yolk, bran, dry milk or wheat, restored the extracted bread to dietary completeness.

27. Osborne and Mendel's Experience with "Artificial Protein-Free Milk."—It has been pointed out that students of normal nutrition failed to make use of the observations of the pathologists during the decade between 1905 and 1915. In discussing the possible explanation of the early failure of their animals fed

isolated food-substances, together with "artificial protein-free milk," Osborne and Mendel (13) emphasized the improvement of the latter by the addition of traces of manganese, iodin, fluorin and aluminum, and dwelt upon the possible importance of minor variations in the inorganic moiety of the diet. Even at the end of 1913 (14) in commenting on McCollum's studies of butter fat they stated that "The added butter fat may have simply supplied something analogous to the so-called vitamines, which Funk considers to be essential for life, and thereby enabled the animals to resume growth on a food thus made adequate for maintenance." Further, "It is still rather early to generalize on the rôle of accessory 'vitamines' when the ideal conditions in respect to the familiar fundamental nutrients and inorganic salts adequate for prolonged maintenance are not completely solved." These quotations will serve to show that these investigators were likewise in the same state of confusion as to the interpretation of the data in the literature of pathology which described the experimental production of beri-beri and of scurvy (15), as were McCollum and his co-workers. At the time Hopkins published his proof of the necessity of certain accessory foodstuffs he apparently was not aware of the epoch-making observations of Eijkman that a diet of polished rice would induce polyneuritis in birds and that the rice polish contained something which would relieve the condition (9).

28. The Confusion Concerning the Essential Nutritive Factors Previous to 1915.—It is easy now to see in the light of later experience why such skepticism existed regarding the necessity of hitherto unappreciated factors in the diet. Osborne and Mendel and McCollum had seen young rats grow for a considerable time when restricted to diets of supposedly pure food substances. These substances, however, always contained a considerable amount of lactose or milk sugar, and it was not appreciated at the time that impurities of a most important nature might still adhere to lactose of a relatively high degree of purity.

When it was found in 1913 that the addition of butter fat promoted growth on a diet, which consisted aside from this fat only of substances of accepted purity, every component of the diet being regarded as known chemically, it seemed very plausible that the only unidentified dietary essential for the rat was associated with the fat fraction. This view was at one time held by McCollum. In all such studies the question as to the degree of purity of each of the ingredients of the diet necessary

to warrant the conclusion that no impurities of a significant nature were present could be decided only through critical and comparative experiments.

29. **How the Problem Was Cleared Up.**—The manner in which the problem was finally cleared up as to the number of unidentified factors the diet must contain in addition to the long recognized fundamental nutrients, protein, carbohydrate, fat and mineral salts, is of historical interest. During the years between 1913 and 1918 Osborne and Mendel, and McCollum and his co-workers confined their researches to different fields. The former two, believing that their diet containing a purified protein and other isolated food-stuffs, supplemented with 28 per cent of "protein-free milk," was satisfactory for the study of the comparative values of the proteins from various sources, extended their investigations in the direction of determining the biological value of each of the more important proteins isolated from natural foods. McCollum and his co-workers turned their attention to the determination of the nature from the dietary standpoint, of the deficiencies of our natural foods. It was through these studies that the next advance was gained in our knowledge of what constitutes a satisfactory diet for the rat.

30. **McCollum's Studies with Restricted Rations.**—While the studies with rations restricted to a single plant source were in progress with cattle at the Wisconsin Experiment Station, McCollum, beginning in the year 1907, restricted the diet of rats to each of the more important single grains and seeds, fed as the *sole* source of nutriment. It was discovered that whole wheat alone, rolled oats alone, maize kernel, or any other seed fed alone, failed to induce any growth in young animals, or to maintain life for a long period of time. It seemed to him in 1913 after the completion of the experimental studies described in this chapter, that he was in possession of the necessary knowledge to enable him to determine the nature of the faults responsible for these failures.

31. **Formulation of the Biological Method for the Analysis of a Food-Stuff.**—Chemical analysis shows the cereal grains to contain all the essential food substances for which we know how to analyze, and it was assumed as a working hypothesis that the only unknown factor contained in the diet was that associated with certain fats. The first intensive study was made on the wheat kernel. It was reasoned that since all the types of nutrients are represented in a seed such as the wheat kernel, except

possibly the unknown one which had been demonstrated to be present in certain fats, the fault or faults of wheat from the dietary standpoint must lie in the *quality* of one or more of these food factors. It was reasoned that valuable data might be secured by enhancing the protein, the inorganic moiety and the fat factors separately in feeding experiments. It seemed possible to discover by means of a systematic series of feeding experiments in which the quality of the seed should be improved with respect to one dietary factor at a time, which factor was interfering with growth (16). Accordingly McCollum and Davis fed the wheat kernel in the following combinations, and obtained the results noted:

1. Wheat alone . . . No growth, short life.
2. Wheat plus purified protein . . . No growth, short life.
3. Wheat plus a salt mixture which gave it a mineral content similar to that of milk . . . Very little growth.
4. Wheat plus a growth promoting fat (butter fat) . . . No growth.

From these results it seemed apparent that either the working hypothesis regarding the factors which are necessary in the diet must be wrong, or there must be more than a single dietary factor deficient in wheat, and jointly responsible for the poor nutrition of the animals. In order to test this theory another series of experiments were carried out, in which wheat was supplemented with two purified food additions:

5. Wheat plus protein, plus the salt mixture . . . Good growth for a time. Few or no young. Short life.
6. Wheat plus protein, plus a growth promoting fat (butter fat) . . . No growth. Short life.
7. Wheat plus the salt mixture, plus a growth promoting fat (butter fat) . . . Fair growth for a time. Few or no young. Short life.

The behavior of the animals fed wheat with two purified food additions was highly suggestive that there are three dietary factors of poor quality in the wheat kernel. This was demonstrated to be true by a feeding trial in which wheat was fed, supplemented with three purified food additions:

8. Wheat plus protein, plus the salt mixture, plus a growth promoting fat (butter fat) . . . Good growth, normal number of young, good success in rearing young. Life approximately the normal span. See chart 2.

McCollum and Davis were, in 1914, more than ever convinced that the only element of mystery in the normal diet was the unidentified substance in butter fat, for with the improvement of three dietary factors wheat became a satisfactory food for the

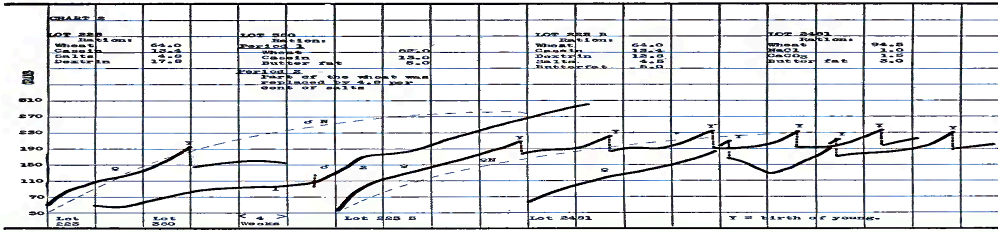

Chart 2.—This series of curves illustrate the nature of the deficiencies of the wheat kernel from the dietary standpoint. Lot 223 lacked sufficient fat-soluble A but was otherwise complete. Lot 380 contained everything which was essential except certain mineral salts (Period 1). In Period 2 the animals became able to grow because of the inclusion of the missing calcium, sodium and chlorin. Lot 223 B grew well and were very fertile and successful in rearing young on wheat supplemented with respect to protein, mineral salts and fat-soluble A (in butter fat). The record of the animal on ration 2481 shows clearly that the mineral deficiencies of wheat are most serious, for without enhancing the proteins of this cereal, good growth and moderate fertility were secured. This curve further shows that only a calcium salt and common salt or sodium chlorid are necessary to complete the inorganic moiety so as to make possible fairly satisfactory nutrition.

nutrition of an animal during growth, and for the support of all the functions of reproduction and rearing of young.

32. **Two New Viewpoints in Nutrition.**—This series of experiments brought to light two new viewpoints in nutrition, one of which was—*that the inorganic content of the wheat kernel, although it furnishes all the necessary elements, does not contain enough of certain of these to meet the requirements of a young animal during the growing period.* It is true that some years earlier Henry (17) had called attention to the deficiency of the corn kernel in ash content and had in some of his experiments added wood ashes to the diet, with noticeable improvement in the well-being of the animals. The fact that seeds, such as wheat, fail to supply enough of any of the essential inorganic elements was not generally appreciated and was given but little attention in books on nutrition. Later, work by McCollum and Simmonds demonstrated that the deficiency in mineral elements in wheat and other seeds is limited to four elements, calcium, phosphorus, sodium and chlorin (18).

A second new viewpoint brought out by these experiments was the fact that the wheat kernel is indeed too poor in its content of the unidentified substance which butter fat contains to nourish satisfactorily an animal over a long period of time.

33. **Proteins Not All Constituted Alike.**—It has already been mentioned that the studies of Kossel, Fischer and of Osborne had made it clear that there should exist very pronounced differences in the value of the proteins from different sources. The proteins were prepared in a state of relative purity and were digested in the laboratory by means of acids, and were analyzed by the methods of Fischer and of Kossel. Certain of the eighteen digestion products, the amino-acids, were determined quantitatively so far as the methods would permit. Although the technique was never perfected so as to give results approximately quantitative, except in the case of less than a third of the amino-acids known to be formed in the digestion of proteins, it was shown in the case of these few amino-acids that there were very great variations in the proportions among them in the mixtures obtained from proteins of different sources. Thus the proteins of the muscle tissues of several species of animals were shown to yield between 12 and 14 per cent of glutamic acid, one of the products of hydrolysis obtained from practically all proteins. The same amino-acid is present in the two principal proteins of the wheat kernel to the extent of about 40 per

cent of the total protein content. These two proteins together make about 85 per cent of the total protein of the wheat kernel. Other equally great differences were shown to exist in the composition of proteins of our common food-stuffs, and those of the tissue proteins formed during growth.

34. **The Problem which an Animal Meets in Its Protein Nutrition.**—A good illustration of the problems which the animal meets in its protein nutrition may be had by comparing the digestion products of the protein molecule to the letters of the alphabet. The proteins of the food and of the tissues may be regarded as made up of the same letters arranged in different orders and present in different proportions. In growth the animal takes as food, proteins which are very unlike those of its tissues, splits these into the simple compounds, the amino-acids, and then, after absorbing these, puts together the fragments in new order, and in new proportions to form the tissue proteins.

If the muscle tissue of an animal be likened to a block of printer's type so arranged as to print the rhyme beginning "Jack Spratt could eat no fat, and his wife could eat no lean," the proteins of which the muscle consists are represented by the individual words, and the protein digestion products by the letters of which the words consist. Now if the animal should take food proteins which correspond to a block of type which would print the jingle beginning "Peter Piper picked a peck of pickled peppers," it is easy to understand that when the proteins of the food are resolved into their constituent letters, and an effort made to form the body proteins of the new and different type from the letters supplied by the food, the transformation cannot be made. In setting up the first line, "Jack Spratt could eat no fat and his wife could eat no lean," we need four of the letter t, but the food proteins contain but one. The first line of the Jack Spratt rhyme, which represents the muscle proteins, requires but one letter p, whereas the food proteins expressed by the Peter Piper rhyme yield nine in the first line. The first line of the Jack Spratt rhyme contains the letters j and n, whereas the Peter Piper rhyme contains none, so that even with the entire stanza:

Peter Piper picked a peck of pickled peppers,
If Peter Piper picked a peck of pickled peppers,
Where's the peck of pickled peppers
That Peter Piper picked?

it is not possible to reproduce even the first line of the Jack Spratt rhyme, and in order that growth might become possible it would be necessary to take proteins of another character which would supply the missing letters.

Such a comparison between food proteins and tissue proteins gives a good illustration of the kind of problem which the animal meets in its protein nutrition. The most conspicuous protein of the corn kernel, zein, is wholly lacking in three of the amino-acids or digestion products which are obtainable from most tissue proteins. In accord with what we should expect on theoretical grounds, this protein is, when taken as the sole source of amino-acids, not capable of supporting growth, or of maintaining an animal in body weight. This illustration shows how we may have superior, good or inferior food proteins for the formation of body proteins in growth.

35. **The Biological Analysis of Polished Rice.**—The investigations, the object of which was to find the cause of the failure of an animal to grow when restricted to wheat as its sole source of nutriment, were carried out in 1913, soon after the publication by Funk of his first work on polyneuritis. In the same year Hopkins called attention to the remarkable effects produced by the addition of small amounts of milk to diets composed of purified food-stuffs. The vitamin hypothesis had just been formulated by Funk (19). McCollum and Davis were, therefore, aware of the relation of a diet of polished rice to experimental beri-beri. They believed, in the light of their experiences with the diet of purified protein, milk sugar, fats and inorganic salts, that such a mixture was capable of inducing growth when certain fats were supplied, but not when others were substituted. The further fact that wheat could be supplemented by purified protein, a growth-promoting fat, and a suitable salt mixture, that is, with food-stuffs of known character, seemed to indicate that there was but a single unidentified substance necessary in the diet. They decided to apply to polished rice the same procedure which had shown so clearly the nature of the dietary deficiencies of wheat. Rice, they reasoned, could be nothing less than a mixture of proteins, starch, fat, and of inorganic salts, similar to that contained in wheat, but in different proportions. It should, therefore, be supplemented with a suitable salt mixture, a purified protein, and a growth-promoting fat, so as to induce growth and maintain animals for a long time in a state of health. This seemed to be a necessary corollary, since they

had secured growth and well-being in animals fed strictly upon a mixture of purified protein (casein), starch, milk sugar, butter fat and a mixture of inorganic salts of suitable composition (20).

It was a great surprise to McCollum and Davis to find that polished rice, even when supplemented with the purified protein, casein, butter fat and a salt mixture properly constituted, failed utterly to induce any growth in young rats (21). Not only did they fail to grow, but in the course of a few weeks they developed in some cases a state of paralysis which was suggestive of polyneuritis. Here was an apparent contradiction. The polished rice could be nothing less than a mixture of protein, carbohydrate, fat and salts. The only difference between this and the mixture of supposedly purified food-stuffs with which they had achieved success was in the 20 per cent of milk sugar which the synthetic diet contained. They, therefore, decided to repeat the experiments with the latter mixture, with the milk sugar replaced by starch. It was found that this change in the composition of the food mixture made the difference between success and failure. No growth could be secured when the milk sugar was omitted. Later experiments showed that if milk sugar sufficiently purified by repeated crystallization was added to the purified food mixture it was no longer effective in inducing growth whereas the water from which the sugar had been crystallized would, when evaporated upon the food mixture, render it capable of inducing growth. This made it evident that there is indeed a second dietary essential, of which an animal needs but a very small amount, but which is absolutely necessary for both growth in the young and for the maintenance of health in the adult.

36. **Demonstration of the Necessity of Two Vitamins in the Nutrition of the Rat.**—Further experiments were then conducted to find whether this unidentified substance which was being added accidently as an impurity in the milk sugar was the same as the substance with which Funk and others were dealing in their studies of beri-beri. It was found that pigeons which had developed beri-beri as the result of being fed exclusively upon polished rice could be temporarily "cured" with any preparation which would, when added to a diet of purified food-stuffs containing a growth-promoting fat, cause animals to grow. See chart 3.

Following the method of Funk and Suzuki, McCollum and Davis in 1914 employed alcoholic extracts of various natural foods, adding the alcohol-soluble matter to the standard mixture

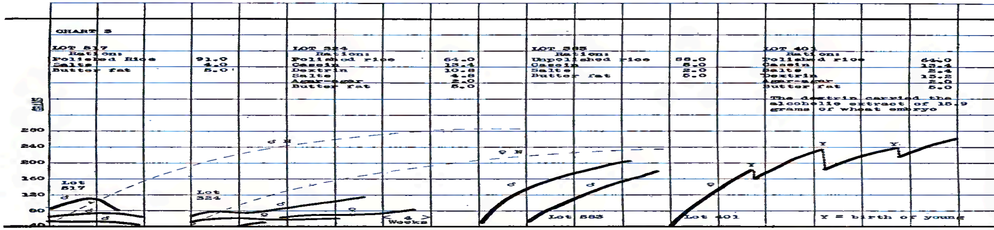

CHART 3.—The four groups of curves illustrate the nature of the deficiencies of the polished rice kernel as a food for the rat. Lot 317 could not grow on rice, a complete salt mixture and butter fat because the anti-neuritic substance water-soluble B was absent. Improvement in the protein by the addition of casein did not enable the animals to grow except to a very slight extent. Unpolished rice contains the germ which is rich in water-soluble B, so the addition of the same supplements as in Lot 317 served to complete it and make a diet on which growth was rapid. Lot 401 differed essentially from 324 in that it contained the alcoholic extract of wheat embryo or germ. This supplied water-soluble B, and therefore enabled the animals to grow, since all other deficiencies of polished rice were made good by the addition of a protein (casein), a complete mineral salt mixture and butter fat which contained fat-soluble A.

of purified protein (casein), starch (dextrinized), salts and butter fat, and soon became convinced that the substance which relieves polyneuritis in pigeons was always present in the preparations which rendered the diet of purified food-stuffs capable of promoting growth. An alcoholic extract of ether extracted wheat germ was finally adopted as a source of this dietary factor in later investigations. Funk and his co-workers had previously shown that the curative substance is present in many natural foods (19). Repeated experiments by McCollum and Davis showed that the inclusion of the alcoholic extract of wheat germ or of other food was not sufficient to induce growth *unless the butter fat or other similar fat was likewise added to the purified food mixture. Both the growth-promoting fat and the trace of unidentified substance in the alcoholic extract of wheat germ are necessary for the promotion of growth or the preservation of health* (22).

37. **Funk and Macallum Report that Butter Fat Contained No Vitamine.**—Funk and Macallum found butter fat ineffective for the cure of polyneuritis in pigeons, and accordingly considered it free from "vitamine." They fed young rats a diet of purified food-stuffs supplemented with a liberal amount of butter fat, and found that the animals did not grow. Although this was the result of the lack of the anti-neuritic substance, they were not at that time clear as to the several factors which are necessary in the diet and interpreted their data as evidence that butter fat possessed no growth-promoting properties (23).

38. **McCollum and Davis Formulate an Hypothesis Regarding the Essentials of an Adequate Diet.**—As a result of these experiments McCollum and Davis (22) formulated in 1915 their working hypothesis of what constitutes an adequate diet. The diet must contain, in addition to the long recognized dietary factors, viz., protein, a source of energy in the form of proteins, carbohydrates and fats; a suitable supply of certain inorganic salts, two as yet unidentified substances or groups of substances. One of these, fat soluble A, is associated with certain fats, and is especially abundant in butter fat, egg yolk fats, cod liver oil and the fats of the glandular organs such as the liver and kidney, but is absent or present in but traces in fats or oils of vegetable origin. The second substance, water-soluble B, is never associated with fats or oils of either animal or vegetable origin. It is widely distributed in natural foods, and can be isolated in a concentrated, but not in a pure form, from natural food-stuffs

by extraction with either water or dilute alcohol. This water or alcoholic extract always contains the substance which cures polyneuritis.

39. **Two Vitamins Necessary for Nutrition of the Rat and Three for Man, Monkey and Guinea Pig.**—This statement of the deductions which it seemed justifiable to draw from the experimental evidence at hand in 1915 can be applied to-day to the nutrition of the rat. It has, however, been found that there exists a third dietary essential which appears not to be necessary in the food of the rat, but is indispensable in the diet of man, monkey and the guinea pig. This is a substance which protects against the syndrome of scurvy. It will be discussed at length in Chapter VIII.

From what has been said of the experimental studies which ultimately led to the conception that there were necessary two uncharacterized dietary essentials in addition to the long recognized food principles in the diet of the rat, it will be appreciated that about 1914-15 there were suggestions of various kinds "in the air," and that the time had arrived when some one of the several investigators working in the field would soon formulate on the basis of definite experimental evidence a working hypothesis concerning the essentials of an adequate diet. Thus in November, 1914, Mendel, in his Harvey lecture, said, "It is not unlikely—to speak conservatively—that there are at least two 'determinants' in the nutrition of growth. One of these is furnished by our 'protein-free milk,' which insures proper maintenance even in the absence of growth. . . . Without this 'determinant' . . . the special components of butter fat or cod liver oil or egg fat induce only limited gains at best. Another 'determinant' is furnished by these natural fats. Either of the determinants may become 'curative'; both are essential for growth when the body's store of them (if such there be) becomes depleted. It is too early to attempt a tenable conclusion" (11).

40. **Stepp Failed to Interpret Correctly His Results.**—Stepp was unable to detect any special dietary property in butter fat, while he could easily do so when alcoholic extracts of certain natural foods were used. This is now readily understandable. His alcoholic extracts contained some of both the uncharacterized substances discussed above, whereas butter fat contains but one. The latter, without a supplementary source of the second one of these dietary factors would permit of failure of the experimental animals.

41. The Biological Method for Analysis of a Food-Stuff Useful in Estimating Vitamins.—The biological method for the analysis of a food-stuff was first developed with a view to discovering the nature of the deficiencies of individual natural food-stuffs. For this purpose the food under investigation is the principal component of the diet and is supplemented with small additions of one or more purified food substances (e.g., protein, inorganic salts, vitamins), in order to bring to light the nature of the additions which enhance its value. The method is applicable in another modification, however, which has yielded much valuable information concerning the relative values of many of our more important foods with respect to any one dietary constituent.

The last mentioned application of the method involves the conduct of feeding experiments in which a basal food mixture is employed which is entirely satisfactory as a source of nutriment for a growing animal except that it lacks entirely a single dietary essential. For example a mixture of purified protein, carbohydrate, an adequate salt mixture and a fat containing fat-soluble A, constitutes a diet which is complete for the rat with the exception of lack of the anti-neuritic substance, water-soluble B. If experiments are conducted with such a food, supplemented with minimal additions of some natural food whose value as a source of water-soluble B it is desired to estimate, it can be determined what is the smallest addition of the food under investigation which will furnish just sufficient of this vitamin to make possible the normal growth and satisfactory maintenance of the animals. This method was first employed by McCollum and Davis (16), who determined that wheat germ was approximately five to seven times as valuable as a source of water-soluble B as is whole wheat or other cereal. Their results indicated that the cereal grains are essentially on a parity with respect to their content of this substance, and are somewhat inferior to alfalfa leaves in this respect. In a similar manner, if the basal diet be made complete except for fat-soluble A, the method may be satisfactorily employed for comparing the content of this substance in a series of natural foods. To this end they are each fed with the basal ration, the amount added being adjusted in a series of experiments so as to find the least amount which completes the ration and induces normal nutrition.

42. The Nomenclature of the Vitamins.—The nomenclature of these recently discovered nutritive complexes is more or less

in a state of confusion. Stepp (12), who is entitled to the credit of having first established the indispensability of certain alcohol-ether soluble substances in the diet, regarded them as lipins. Funk (19) designated a hypothetical group of protective substances of unknown nature "vitamines." Hopkins (9) after discovering the remarkable growth-promoting effects of small additions of milk to a diet of purified food-stuffs, termed them "accessory" food substances.

There is much reason to believe that Stepp's view that the substances under discussion are lipins is erroneous. They are associated with the lipins under the conditions under which he worked. The term "vitamine" seems to bestow an importance upon these substances paramount to that of other indispensable substances. Such an assumption is obviously unwarranted. There is no evidence as yet that any of them are amines, and indeed there are strong reasons for believing that one at least, that associated with certain fats, does not contain nitrogen. The term amine has a definite significance in organic chemistry, and it seems reasonable to insist that its use should be reserved for compounds containing an amino group. The term "accessory" food-stuffs is the least desirable of all, for it uses the term "accessory" in a sense exactly the opposite to its well established meaning, that of an agent acting in a subordinate way to a principal agent. There can obviously be no room for differentiation on a basis of importance among a series of indispensable food complexes which includes several amino-acids, nine inorganic elements, a utilizable carbohydrate, and two or more unidentified factors. The term "accessory" would be rightly used to designate the condiments, such as the various spices, which add to the acceptability of foods.

When it was established that there are two unidentified factors necessary in the nutrition of the rat; that one was soluble in fats and not in water, and the other never associated with fats, but easily dissolved out of natural foods by water or dilute alcohol, it became necessary to differentiate between them by names which would characterize them. For the reasons stated, none of the terms in use seemed desirable, and it seemed to McCollum and Kennedy (24) advisable to employ provisionally algebraic terms, using a prefix designating characteristic solubility. They proposed the terms fat-soluble A for the factor carried by certain fats, and water-soluble B for the factor which relieves the paralysis in polyneuritic animals. These terms have found

widespread acceptance, but the terms introduced by Stepp, Funk and Hopkins, are still used by many, and frequently in ludicrous combinations, such as fat-soluble A vitamin; water-soluble B accessory. The lack of appreciation of fitness, and even of consideration of definition of well-established terms, which is exhibited by certain writers of this branch of literature is truly amazing.

Upon the establishment of the existence of an anti-scorbutic substance Drummond (25) designated it water-soluble C. He has recently (26) suggested that the spelling of vitamine, be changed to vitamin, and this term be adopted to designate the entire group of chemically uncharacterized dietary essentials. This would be in accord with the nomenclature of the hormones and of the alkaloids, and indicates nothing of their chemical natures. This seems to be a satisfactory nomenclature to adopt.

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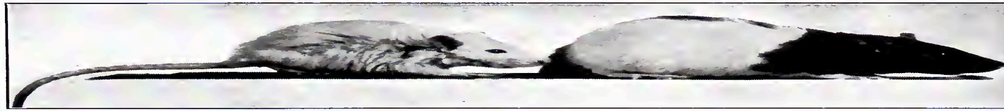

FIG. 5.—The rations of these two rats from weaning time were exactly alike except in the character of the fat which they contained. The one on the left was given 5 per cent of sunflower seed oil. The one on the right was given 1.5 per cent of butter fat. Butter fat, egg yolk fats and the leaves of plants contain a dietary essential, the chemical nature of which is still unknown, which is necessary for growth or the maintenance of health. This substance is known as fat-soluble A, and is not found in any fats or oils of vegetable origin. A lack of this substance in the diet causes the development of a peculiar eye disease known as xerophthalmia. The animals were the same age when photographed.

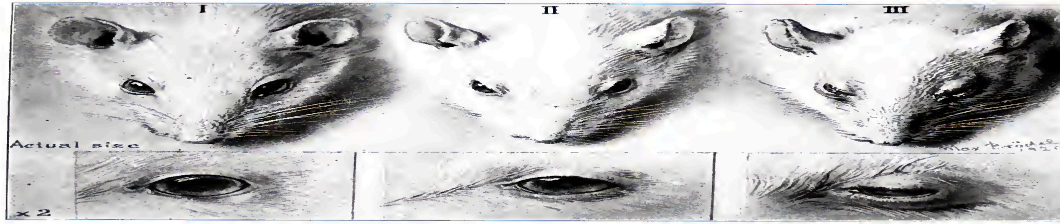

FIG. 6.—Illustrates the appearance of the exterior of the eyes as ophthalmia of dietary origin develops. On the left is shown the normal eye of the rat. In the center is shown the puffiness around the eyes which denotes that ophthalmia is about to appear. On the right the extreme edema of the eyelids is shown. When the latter condition is reached the cornea usually ulcerates and a bloody exudate seals the lids shut. The eyes become filled with leucocytes. The introduction of a fat containing fat-soluble A leads, in the earlier stages, to prompt recovery from this condition.

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CHAPTER III

THE EARLIER VIEWS OF NUTRITION PROBLEMS

43. **Dr. Beaumont's Views on Digestion.**—Although food constitutes the chief item in the expense of living among the wage-earning class, and is more intimately concerned with the promotion of health and strength than are clothing, shelter and climate, it is only very recently that any serious thought has been given to the nature of food, and to the processes which it undergoes in being utilized for the bodily upkeep. Man has adjusted himself to such food supply as he found available, and accordingly latitude, climate and soil and proximity to large bodies of water have been the determining factors in establishing his dietary habits. Common observation led to the knowledge that people in different regions lived on diets of widely different character, yet without any markedly different success in physical development. Indifference to the nature of the food supply, except as to palatability, was therefore natural, since there was no obvious evidence that the character of the diet had anything to do with well-being, provided a sufficient amount of food could be had.

The paucity of our knowledge concerning nutrition that existed toward the middle of the nineteenth century is well illustrated by the views of Dr. William Beaumont, a surgeon in the United States Army, expressed in his book, "Physiology and Experiments," published about 1832. He had the good fortune to study the processes of digestion with the hunter, Alexis St. Martin, who had a fistulous opening into the stomach as the result of a gunshot wound. Beaumont collected gastric juice from his subject's stomach and studied its effect on various foods. He also introduced foods into the stomach and observed through the opening, the behavior of this organ during digestion. He stated very definitely that he believed that the views of others to the effect that there are various kinds of nutrient substances, were in error. In his opinion there was but one kind of food or "aliment" as he termed it. This was, he believed, present in all

foods, and was simply dissolved out by the action of the gastric secretion. Dr. Beaumont was one of the most progressive investigators of his time (1).

The chemistry of both inorganic and organic substances advanced with great rapidity during the nineteenth century, and among the facts which were established was the widespread occurrence of proteins, carbohydrates and fats as components of foods, thus disproving the view that there was but "one kind of aliment." Of these nutrient principles only the first named contains the element nitrogen. It is the oxidation of these food substances that yields the energy which keep the body warm, and enables it to do mechanical work. The laws governing energy metabolism were next developed.

44. Lavoisier Placed Nutrition on a Scientific Foundation.—The modern era of the science of nutrition may be said to have been introduced by the famous French scientist, Lavoisier, in 1780. He was the first to apply the thermometer and the balance to the study of the chemical changes taking place in the living body. He established the fundamental fact that the production of heat involved the combination of the oxygen of the air with the substances taken into the body as food, and was in fact a process of combustion. He discovered that the temperature of the air had a pronounced influence on the rate at which substances in the body were oxidized. It is slow at temperatures which we find comfortable with light clothing, and is greatly accelerated by cold. Exercise, he found to stimulate combustion in the body, and he also observed that during work it might rise to several times the resting metabolism. These fundamental facts established by Lavoisier have formed the subjects of numerous investigations, which greatly increased our knowledge of detail in this important field.

About 1842 Joule described experimental data establishing the mechanical equivalent of heat. Heat is measured in terms of the calorie, which is the amount of heat necessary to raise the temperature of 1 cubic centimeter of water 1 degree centigrade, or one pound of water 4 degrees Fahrenheit. Another unit, the large Calorie, is 1,000 times the small calorie. The rate at which energy metabolism varies with the activity of the individual, and in the absence of suitable clothing, with the temperature, is the most spectacular phase of the metabolic processes, and is easily observed. A man at rest may have need of only about 1,600 calories a day in the form of suitable food, in order to cover his

energy requirements. The same man at very severe labor may require 10,000 calories a day. It is not surprising that this obviously important phase of metabolism was early studied in great detail.

In 1866, Pettenkofer and Voit in the University of Munich, began the publication of their elaborate studies on energy metabolism carried out with the aid of a respiration apparatus by means of which they could measure accurately the amount of oxygen absorbed, the amount of carbon dioxid and of water in the products of respiration and the heat given off by the body under various conditions (2). They introduced into their experimental work the idea suggested by Liebig in 1842, that the nitrogen eliminated in the urine could be made a measure of the amount of protein destroyed in metabolism, since protein is the one prominent food-stuff which contains this element. Pettenkofer and Voit studied the metabolism of fasting men and dogs, and of the same subjects when taking different kinds and amounts of food. From the magnitude of the "respiratory quotient," which is the figure obtained by dividing the volume of carbon dioxid eliminated by the volume of oxygen consumed in respiration $\left(\frac{CO_2}{O_2}\right)$, it was possible to decide what kind of food was being oxidized as a source of energy in the body. When carbohydrate is burned the quotient is 1. When fat is burned it is 0.7, and when protein is burned the figure is approximately 0.8. They found that a dog could be maintained in nitrogen and energy equilibrium during a period of a few days on a diet of protein alone (muscle tissue).*

45. **The Specific Dynamic Action of Food-Stuffs.**—The early studies relating to energy metabolism led to the discovery that the protein of the food differs in one marked respect from either carbohydrate or fat, by its great stimulating effect upon metabolic processes as measured by the rate of oxidation. This is illustrated by the following type of experiment: If a dog is observed when it has been for some hours without food, and the rate of energy metabolism carefully measured, it will be found that this remains constant within narrow limits so long as the animal remains at rest. If now it is fed liberally with either fat or carbohydrate and the observations on its energy metab-

* For a detailed history of this important phase of nutrition, the reader is referred to "The Science of Nutrition," Graham Lusk, 3d Ed. Philadelphia, 1917.

olism are continued, there is observed a slight increase in metabolism which is the direct result of the utilization of these foods. If on the other hand, a liberal portion of protein rich food, such as meat is fed to the animal instead of the non-nitrogenous nutrients, there is a surprising acceleration of the metabolic processes, attended with a marked increase in energy set free within the tissues. This was first shown by Bidder and Schmidt in 1852. Their experimental animal was a cat. During a certain interval of time the animal used 50.18 grams of oxygen and eliminated from its lungs 53.52 grams of carbon dioxid. The animal was then allowed to eat all the meat it would consume and the observations continued. During a similar interval the cat used 103.84 grams of oxygen and respired 113.52 grams of carbon dioxid (3).

46. **Energy and Protein Were Long Regarded as the Most Important Factors in Nutrition.**—The remarkable researches of Voit, Pettenkofer, Rubner, Atwater, Lusk, Zuntz and Benedict on the metabolism of matter and energy in the body attracted deserved attention and for years occupied a large area in the field of vision of students of nutrition. The researches were extended to the study of some of the finer problems of metabolism. It was shown that carbohydrate can be converted into fat by the tissues, and that a part of the carbon which the protein molecule contains can be converted in the body into glucose. These investigations shed much light on such conditions of perverted metabolism as prevent the oxidation of sugar in the tissues (diabetes). In the light of the new developments in the chemistry of proteins and their digestion products, the amino-acids, Lusk finally explained in great measure, the cause of the specific dynamic action of proteins (4).

It was not until after 1900 that the view began to develop that differences in chemical composition brought forth great differences in the nutritive values of proteins from different sources. Previous to that time it was believed by those who were interested in the nutrition of man and animals, that the results of a chemical analysis were of the greatest importance in showing the nutritive value of any food, and on the basis of such analysis, advice was given as to the manner in which foods should be combined. The chemical methods in use at that time were first described in 1864 by Henneberg, and were adopted by the German Official Agricultural Chemists, and afterwards used by food chemists all over the world.

47. **What a Food Analysis Is Intended to Show.**—The food analysis consisted in the following determinations: The nitrogen content, from which the protein was calculated by multiplying the value found by 6.25, on the assumption that all proteins contained approximately 16 per cent of nitrogen; the fat, by extracting the food with some solvent, usually ether, and weighing the amount of substance which was extracted from a known amount of food; the "crude fiber," or cellulose, by treating a sample of the food with a solution of acid and then with one of alkali sufficiently strong to dissolve all components except the more resistant forms of cellulose, and a small amount of mineral matter which this cellulose retained; the ash, or mineral matter, by burning a weighed sample and subsequently weighing the residue left after incineration. The analysis was made on a sample of food which was carefully dried to constant weight in order to free it from moisture. The sum of the protein, fat, ash and fiber, was then subtracted from 100 to give a figure which was designated "nitrogen-free extract." This was assumed in calculations used in estimating the amount of food necessary to meet the requirements of an individual as being essentially a measure of the amount of utilizable carbohydrate contained in the food. Such in outline is the chemical analysis of a food. It will be seen later that the biological method of analysis is very essential to complete our knowledge of the nutritive value of foods.

By 1900 very careful determinations had been made of the amount of heat liberated when a definite weight of the food is burned. This was known as the calorific or fuel value. Numerous determinations had been made of the amount of energy required for a man of ordinary size, per day, when at rest and when doing several kinds of work representative of moderate and more severe kinds of labor. The illustration most widely used by writers on nutrition, was that of comparing the body to an engine, in which fuel (food) was burned and by which mechanical work was performed, with the liberation of a certain amount of waste energy in the form of heat. The adjustment of the supply of calories, or energy units of food, to the needs of the individual, and the amount of protein necessary to make good the "wear and tear" of the tissues, which is an unavoidable result of the life processes, were considered as the two factors of prime importance in the planning of the diet.

48. **Elements of Weakness in the Standard Food Analysis.**

—The standard food analysis regarded of so great importance, had a number of shortcomings, as a method of determining the nutritive value of a food. By means of it the great differences in the make-up of the proteins, which give them very unlike value in nutrition, were not revealed. Protein from one source was assumed to be as good as that from another. Beans and peas, for example, contain about 23 per cent of protein, and compare favorably in this constituent with lean meat. These legume seeds were regarded for many years as essentially the equivalent of meat as a source of protein. They were sometimes spoken of as "the poor man's meat." We now know that the proteins of these seeds have peculiarities in their composition which make them of relatively low value in nutrition when they serve as the sole source of protein in the diet, or when they are combined with some of our most important food grains. Meat proteins are decidedly superior to them as supplements to most of the proteins of our vegetable foods. This was only brought to light by later investigations.

The analysis of foods for their carbohydrate content was not effective as a means of arriving at a decision as to the energy value of this portion of their substance. Man and animals can use starch and sugars as a source of energy, but not cellulose or hemicelluloses. The best method for differentiating between the several types or carbohydrates was that based on the ease with which they are converted into glucose or other simple sugars by the action of acid of certain concentration. The true celluloses, of which paper is made, are not dissolved by the reagents used in food analysis, and could be filtered off, washed, dried and weighed. There are many kinds of vegetable foods which contain considerable amounts of hemicelluloses, a class of carbohydrates which are easily converted by the action of acid into simple, soluble sugars in the process of analysis. Accordingly, these were estimated as part of the fraction called "nitrogen-free extract," and were, in the absence of specific data as to their digestibility, estimated in calculations of dietaries, as the equivalent of starch or sugar.

Hemicelluloses are not acted upon by the digestive secretions of man or animals. They have, therefore, no food value except that imparted to them through the agency of certain microörganisms inhabiting the digestive tract. These organisms may bring about their fermentation with the production of such organic substances as acids and alcohols as intermediary products. These

may be absorbed and utilized by the body as a source of energy for mechanical work or for heat production.

The method for the estimation of fat in food-stuffs was fairly satisfactory, but the materials weighed as fat always contain waxes, cholesterol, chlorophyll, etc. These, with the possible exception of chlorophyll, have no food value, and are inert and chance components of the diet. The fats and carbohydrates were regarded as essentially sources of energy for work or for heat production, and were rightly considered as being able to replace each other in the diet in isodynamic quantities. One gram of carbohydrate or of protein has a caloric value of about 4.1, while 1 gram of fat has about twice this fuel value.

The mineral content of a food-stuff was determined in the standard method of analysis by burning a weighed sample in a dish of known weight. After the organic matter was all destroyed, the dish was cooled in a dry atmosphere and reweighed. The difference between the weight of the dish and the dish plus the ash gave the weight of the mineral matter. Little significance was attached to the inorganic content of foods until recent years, for it was assumed that, since all the elements which are required by the body are found in all foods, the amounts might vary considerably and still meet the needs of the body. In special cases the deficiency of a food in a particular element was so pronounced that it attracted attention. Thus milk is especially poor in iron, and since this element is a constituent of the hemoglobin of the blood, it was early recognized that a young child should not be too long confined to an exclusive milk diet, but should be given some food which would supplement milk in this respect.

49. Proportions Among the Mineral Elements in Food Long Regarded as of Little Significance.—It was not possible to determine the adequacy of the content of our common foods in any of the inorganic elements until exact studies had been made to determine the efficiency of the animal body in absorbing and in conserving its supply. The variations in the inorganic content of the blood in health and disease are so small as to escape observation by any but the most modern and refined methods. Yet these variations are of great significance to the welfare of the individual. Unwarranted assumptions were made by the earlier students of nutrition, concerning the ability of the intestines to absorb mineral salts in a selective way so as to lead to the utilization with high efficiency those elements present in the food in small amounts. The capacity of the kidney to hold

back those elements which are present in the food in minimal amounts and therefore reach the blood in amounts below the optimum was over rated. It is now known that the efficiency of the kidneys in preventing the passage of inorganic salts into the urine along with the waste products of metabolism, is not so great as to protect the body from losses which may be injurious to it when the food contains as little of such salts as those of calcium, phosphorus, sodium and chlorin as are contained in some of our most important cereal grains, tubers and meats. There are well defined limits to the degree to which the intake of these salts can be restricted without causing damage.

50. **The Objective of Students of Digestion.**—It was fully appreciated by students of nutrition many years ago that the food analysis had its serious limitations, and the belief prevailed that the way to eliminate the defects of chemical technic, was to supplement the data obtained by chemical methods with information secured by actual trials to determine the digestibility of foods. The subject and the diet having been decided upon, samples of the food to be eaten were carefully analyzed to determine their content of protein, fat, ash, moisture and "nitrogen-free extract." The period of the experimental trial varied considerably, but in most cases it covered three days. It was customary to keep the subject on a milk diet during a fore period, so that the feces derived from the experimental diet would be different in appearance and could be accurately separated. The chemical constituents of the ingested food minus the amounts of each which appeared in the fecal residues, afforded the data from which the digestibility of the protein, fat and carbohydrate were calculated.

There were some errors in this procedure. In addition to the food substances which escaped digestion, a part of the nitrogen and salts eliminated from the intestine were derived from the secretions of the digestive glands, and from the cellular elements which came from the intestinal mucosa. The quantity of secretions eliminated from the tract depended in great measure on the content of indigestible cellulose in the food. This acted as a sponge, and retained liquids so that they could not be reabsorbed. An animal which is fed a diet containing just sufficient protein to meet its needs, may easily be made to suffer a nitrogen deficit by including in its food supply a liberal amount of cellulose or other indigestible carbohydrate such as are abundant in many vegetables.

In interpreting the results of digestion experiments "utiliza-

tion" of the several components of the food was assumed to be measured by the extent to which they disappeared from the digestive tract. That such an interpretation is not always justified is readily understood. A diet of cereal grains will be well digested and absorbed, but the substances which reach the blood and tissues are not a satisfactory pabulum for the nutrition of the body. Some complexes which are indispensable to the body are present in too small amounts to admit of the utilization of the other useful ones which are abundant, but cannot serve a useful purpose unless they can be used to form definite structures, no unit of which can be dispensed with. Such a food supply may be well absorbed but not *assimilated*. Utilization is an unfortunate choice of a term in this sense for it is liable to be misinterpreted. Knowledge of the digestibility of food-stuffs is of value to students of nutrition, but the idea of quality in the array of digestion products must not be lost sight of.

51. **Limitations of Value of Chemical Composition and Digestibility of Foods.**—It will be appreciated in the light of what has been said that the chemical analysis of a food, and knowledge concerning its digestibility, even when its palatability is satisfactory, do not give any information concerning its physiological effects. These can be discovered only by observations on the well-being of men or animals restricted *during considerable periods of time* to a definite type of diet. It was for a long time assumed, and without any experimental evidence in support of the assumption, that any diet which complied with the composition of ordinary combinations of foods, which experience had shown to be palatable and wholesome components of the diet, and was so constituted as to furnish the necessary amount of protein and of energy in digestible form, would promote growth and prolonged well-being if available in sufficient quantities. This popular conception we now know to be far from true.

52. **The Study of Supplementary Foods in Animal Production.**—It gradually became the custom in Agricultural Experiment Stations to compare the effects of certain combinations of foods on the growth of young animals, and on milk production in cows. These experiments showed plainly that all rations of similar chemical composition are not alike in their physiological effects. In no instance was it possible, however, because of lack of knowledge of the several factors which enter into the normal diet, and because of the faulty planning and conduct of many of the experiments, to interpret the nature of the causes which determined their outcome. These belonged to the type of *im-*

mediate utility experiment and were fostered by agricultural experiment stations because of their practical nature. They were of very great economic value since they showed clearly that certain combinations of foods were either poor, good or excellent for the nutrition of animals. The experiments were not, because of the nature of the food-stuffs employed, and because of the simple mixtures which were monotonously fed to the animals, of such a nature as to make possible deductions applicable to problems of human nutrition. Much of this experimental work was done by men with little scientific training. The experiments were therefore very poorly controlled with the result that much confusion prevailed. Instances were not infrequent where the title of a paper would lead one to believe that the experiments were designed to determine the efficiency with which a certain protein-rich concentrate supplements each of several cereal foods in the nutrition of growing swine, but a careful inspection would show that the ration described was fed to animals allowed to run on a pasture, and eating freely of a forage plant, or given such a skim milk supply as the dairy department afforded. But no account was taken of these factors in the interpretation of the results.

53. **The Conception of Specific Effects of Different Nutrients.**—In 1900 nutrition studies made for the purpose of solving the problems of economic animal production had developed the conception of the specific effects of different foods on the development of the body during growth, and for the performance of work or the production of milk, wool, etc. The skilled animal husbandryman was distinctly in advance of the human physiologist or the medical man in his knowledge of nutrition from the practical standpoint. Professor Atwater, who represented the most advanced thought of his time, wrote, in 1895, his "Chemistry and Economy of Food" (5), which clearly reflects his view that if we knew the composition of all the food-stuffs entering into the human diet, as determined by chemical analysis, their digestibility, and energy values, and the energy requirements of an individual at rest and when doing various kinds of work, we should have all the necessary data to enable us to plan a highly satisfactory nutritive regimen. The well-balanced diet was one in which the proportions among the several recognized nutrients corresponded with the standards adopted as the result of statistical studies of what people in different circumstances and in different localities were selecting for their food supply when guided by the appetite and by expenditure.

54. **Efforts to Study Food Requirements by Statistical**

Methods.—These dietary studies were all made after the plan introduced by Voit in Germany. Atwater made numerous studies of American dietaries, including the homes of laborers, professional men, students and others. Much interest was manifested by the public in these results and others took up similar investigations so that we have available the diets of people in all parts of the country and in all walks of life during the period from 1890 to 1900. The diets of Alabama negroes, Mexican laborers in New Mexico, students in boarding clubs, families of faculty members in several universities, Maine lumbermen, foreign families of various nationality as well as workingmen's and professional men's households were subjected to scientific scrutiny. The quality of any dietary was evaluated by comparison with the standards adopted by Atwater and Voit for energy and protein. This great body of studies were for the most part published in bulletins of the United States Department of Agriculture. Their collection represents an epoch in the development of knowledge of human nutrition.

55. **A Mistaken Idea Regarding Economy in the Purchase of Foods.**—When our knowledge of nutrition had advanced to this point it was natural that the idea of economy in food should attract a great deal of attention, because on the average, a half or more of the family income is spent for food. In the household of a wage-earner food is the largest single item in the family budget. Dr. Atwater made some calculations concerning the amounts of protein, fat, carbohydrates and fuel values which could be purchased for twenty-five cents. These results made it clear that at that time (1884) this sum in Massachusetts would buy one-sixth of a pound of protein, one-fifth of a pound of fat, and 1,120 calories of energy if expended for sirloin steak. The same amount spent for oysters at 50 cents a quart purchased one ounce of protein, two ounces of total nutrients and 230 calories of energy. In buying wheat flour at seven dollars a barrel the twenty-five cents would pay for six and a quarter pounds of nutrients containing eight-tenths of a pound of protein and 11,755 calories of energy. Since it was accepted that the quality of each of the nutrients from each of these foods common in the American diet, was essentially the same, the logical course seemed to be to buy the cheaper articles when economy was essential. There was no fear that any diet would prove unsatisfactory provided it contained sufficient protein and sufficient available energy.

It was pointed out by Atwater that the price of food was not regulated solely by its nutritive value, but that agreeableness to the palate or to the fancy was a factor of great significance in determining the market price. There was at that time, and even after the year 1900, no appreciation of the peculiar worth of certain foods as supplements to others. Nor was there any appreciation of the differences in quality of foods such as we now fully recognize. The astonishing fact that certain lists of common foods do not maintain satisfactory nutrition even though they have collectively a chemical composition exactly similar to those of another list which is satisfactory for the promotion of nutritive well-being did not become appreciated until about 1915.

56. **The Idea of Physiological Economy in Nutrition.**—It is the great merit of Professor Chittenden of Yale University to have introduced into nutrition studies the idea of physiological economy in nutrition (6). Numerous dietary studies in Europe and America had shown fairly accurately what the people in several countries were eating, and the amounts and the chemical composition of the foods had been carefully determined. The most notable students of this subject were Voit in Munich, and Atwater in America. Voit came to the conclusion that an adult man weighing 70-75 kilos and doing moderate work requires 118 grams of protein daily, 56 grams of fat and 500 grams of carbohydrate, the diet furnishing 3,000 calories of energy. Atwater's standard called for 120 grams of protein. These standards were based upon statistical studies of large numbers of people. It was assumed that appetite and instinct were safe guides to the physiological needs of the body.

These standards were arrived at through studies of the actual consumption of food by families in various walks of life. Those who accepted them as the amounts of the various food components which the body requires under specified conditions, accepted the view that man, when in a position to select his food from a suitable variety such as exists in times of relative plenty and moderate values, would take under the guidance of the appetite such amounts of food as are best suited to his bodily needs. Dr. Chittenden was the first to seriously question this doctrine of instinctive selection. He applied what seemed at the time to be a crucial test for the trustworthiness of this doctrine. He restricted men over a period of nine months to diets, the protein content of which fell far below the amount which physiologists generally had accepted as the actual need.

Dr. Chittenden began cautiously experimenting on himself to discover how low he could reduce the protein in his diet without interfering with his well-being, and to his surprise he remained in nitrogen equilibrium and in improved physical condition on a diet which contained only sufficient nitrogen of a digestible and absorbable nature to make the nitrogen content of the urine average 5.699 grams daily over a period of nearly nine months. This corresponds to about 36.72 grams of digestible protein. Dr. Chittenden felt convinced that this reduction of the intake of protein to approximately one-third of the accepted standard requirement for the human body resulted in marked improvement in physiological well-being. He determined to test this question on a scale which would afford convincing evidence, in order that mankind might profit by what was believed to be a great discovery, that physiological economy in nutrition is a matter of great importance for the maintenance of strength and vigor.

57. **The Basis of Chittenden's Views.**—The reasoning by means of which the good results of this abstemious diet, and especially of the low protein intake, were accounted for is interesting indeed. A diminished intake of protein leads to a decreased formation of crystalline waste products, such as acid potassium phosphate, uric acid and the purin bases and other end-products of nitrogen metabolism. These are in part responsible for the sensation of fatigue when they accumulate in the blood. The energy of work comes not from the degradation of muscle substance, but from the combustion of non-nitrogenous food-stuffs such as sugar and fat, and it is not, therefore, necessary to take large amounts of protein food for the purpose of replacing the wear and tear quota, for the latter is but of small magnitude even in severe work. Protein stimulates body metabolism in general, and hence will lead, when taken in excessive amounts, to a rate of metabolism far in excess of the normal amount which results from a diet lower in this factor. This augmentation in the metabolism of the body tissues leads to a waste of energy-yielding substances which might otherwise be conserved for useful expenditure.

It was noted by Dr. Chittenden that while on the low protein diet there was not a single day during the nine months when his urine was turbid, whereas on a rich protein diet it was necessary to take a large amount of water in order to prevent the kidneys from becoming clogged. It was reasoned that this low protein regimen should relieve the kidneys of a burden and would tend

to aid them in maintaining their functional capacity unimpaired.

In order to demonstrate in a large way the importance of his new views, Dr. Chittenden secured the coöperation of a group of his colleagues in the faculty of Yale University and a group of volunteers from among the students. These men were allowed a free choice of food, but they conscientiously adhered during the period of the experiment to the regulations which were imposed on the test. A group of soldiers of the United States Army was detailed under the command of a sergeant to participate in the experiment. The diet afforded to these men was similar to that taken by those who volunteered to subsist on a diet low in protein and of a somewhat abstemious character.

In the case of the faculty and student groups the diet chosen contained but little or no meat, and this automatically tended to lower the protein intake to a decidedly low level. In all cases there was free choice of food in these two groups.

There was no indication that the men who participated in this experiment were not in excellent physical condition at the end of the nine months during which they were nourished on an abstemious although somewhat more liberal diet both in energy and protein than that which Dr. Chittenden had himself taken with apparent benefit. The conclusion was drawn that the general standards of food consumption of people were faulty. The faults in the ordinary diet lay in the excessive consumption of food and especially of protein. The view seemed sustained that the body is better nourished when the amount of food metabolized closely corresponds with the minimum which is necessary to cover its requirements. This better nourishment was held to be due to the relief of the digestive organs and the organs concerned with the transformation of protein food, especially the liver, as well as the organs of excretion, the kidneys in particular, from an excessive burden to which the ordinary eating habits of man subject them.

There can be no doubt that the diets which these men took did not lead to any observable deterioration in their physical well-being. All practically maintained their body weights, or at least lost only such amounts as would be anticipated as the result of the physical exercises some of them indulged in during the test. Their strength increased during the experiment where records were taken and all were said by their observers to be in a normal and healthy condition at the end of the experiment.

58. Crichton-Browne's Views on Parsimony in Nutrition.

—Chittenden's conclusions were not accepted by many students of human nutrition. A critical discussion of his experimental data and conclusions was presented by Benedict (7). He interpreted the digestion data obtained with the soldiers with whom Chittenden experimented, as indicating that the low protein intake had influenced adversely the absorption of protein from the alimentary tract. He further called attention to the fact that animals fed low protein diets do not thrive so well as on more liberal quantities. Benedict pointed out, as did Sir James Crichton-Browne, that dietary studies all over the world had shown that in civilized communities where productive power, enterprise and civilization are at their highest, man has instinctively and independently selected liberal rather than small quantities of protein (8).

It should be stated that in 1917, when there was a food shortage brought about as the result of the World War, Benedict conducted an experiment on twelve men, all students of the Y. M. C. A. College at Springfield, Mass., to see what the effects would be of rapidly reducing the body weight by about 10 per cent by a sharp reduction in the amount of food ingested. This was accomplished in four to six weeks. Thereafter the food consumption was so regulated as to maintain the weight at the new level. Each man lost approximately 150 grams of nitrogen, equivalent to about a kilogram of protein. Their metabolism was, therefore, reduced to a distinctly lower level than normal during the greater part of a school year. From the results of his observations he was led to modify his former view and to become a convert to the idea that the abstemious diet best promotes physical well-being (9).

59. **Older Experiments Not Satisfactorily Planned to Give Results of a Conclusive Nature.**—The question naturally arises how far are we justified in drawing conclusions from the data furnished by these experiments on the point of whether this is a satisfactory regimen to which man may safely adhere throughout the adult period of life. It must be admitted that in the light of the new viewpoints which have been illuminated by animal experimentation during the past decade, these results on men do not seem sufficiently convincing to warrant any conclusions relative to the most important of all questions which arise in the life of the individual, that of maintaining to a late period in life the full vigor of youth.

These experiments on men covered approximately 1 per cent

of the normal span of life for individuals of their age. It has been abundantly demonstrated on animals that diets which fall far below the standard of quality necessary to maintain life and vigor over a very great fraction of the span of life of which the species is capable of living, may cause no noticeable deterioration in the physical condition, during even 5 per cent of the normal expectation of life. In order to produce noticeable effects by faulty diet during 4 or 5 per cent of the average life, it is necessary that the faults shall be relatively severe. Yet diets which are just good enough to permit a young animal to develop in what appears to be an approximately normal manner, may cause early aging, and instability of the nervous system. Either during youth, while growth is still in progress, or after it has ceased, the adherence for even brief periods of a few days or weeks to a diet which is unsatisfactory in some degree, leads to a deviation from the normal histological structure of the osseous, the nervous or the circulatory tissues, depending upon the nature and extent of the faults in the food. Such abnormal modification of tissue structure, would ordinarily escape observation even to-day, and certainly a few years ago.

60. **Effects of Faulty Diets on the Life History of Animals.** —Let us illustrate the principle we have in mind by the results of animal experimentation. McCollum, Simmonds and Parsons (10) restricted a large number of groups of young rats to diets which were faulty in different degrees with respect to the quality of their protein content. The experiments included the period of growth, and of adult life at least to the point of marked development of senile characters. The fertility and success with the nursing of young, the stability or instability of the nervous system as shown by indifference to being handled, which is characteristic of the well-nourished rat, or the apprehensiveness and timidity of the malnourished one, were carefully observed, etc. Successive generations of the same families, where young were reared, were maintained on the family diet. These experiments will be discussed more in detail in a later chapter, but it may be stated here that the deviation of the quality of the protein moiety of the diet even in slight degrees from the optimum, exerts a profound influence on the *life history* of the animals and on the *functioning of the nervous system.*

It may be added that the faults of a diet need be no more pronounced than are encountered in a mixture consisting of cereal grains, legume seeds, tubers, fleshy roots and muscle meats, to

produce profound physical deterioration when such a regimen is adhered to over any considerable period.

61. Longest Experiments on Man Have Not Exceeded 5 Per Cent of the Possible Life Span.—The Experiments of Chittenden and of Benedict covered but approximately 1 per cent of the expectation of life of the young men who served as subjects. They can scarcely be expected to be used as a basis of deductions of a far-reaching nature concerning the dietary practices which man may safely adhere to throughout long periods. Our conclusions as to what is safe or unsafe must be arrived at through tests of special types of diets on animals, the life histories of which are carefully observed, and the vitality of whose offspring is carefully compared with a satisfactory standard of excellence, and the correlation of these results with the experience of man in various parts of the world, where groups are found whose dietary habits are of peculiar and restricted types. Such data will be set forth in later chapters of this book.

62. "Optimal" a Better Goal Than "Normal" in Planning the Human Diet.—The studies of McCollum and Simmonds have introduced into the philosophy of nutrition the idea that the word "normal" is too indefinite a term, and less satisfactory than "optimal" to designate the standard of excellence toward which we should strive in respect to physical development. They emphasize that our standards of what constitutes normality are based upon common observation rather than upon the best possible achievement as illustrated by the best specimens in the population. These investigators also pointed out that it is unsafe to judge by the appearance or feelings of a man or animal under special conditions during a relatively small fraction of life, especially that part in which recuperative power and endurance are greatest, that a dietary regimen which has proven unsafe for the promotion of vigor and health in animals, is safe for man. Physical deterioration may, and generally is unnoticed or not admitted until it is pronounced. It is important to appreciate that in the aggregate, it is borderline states of malnutrition, characterized by a condition of nutritional instability, that is the greatest menace to the individual when his health and efficiency over the life period is considered.

With this attitude toward the subject of our discussion, we may now turn to some of the more technical phases of nutrition investigations, the results of which have served as a basis of practical conclusions of great value for the health of man.

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CHAPTER IV

THE NUTRITIVE VALUE OF THE PROTEINS FROM VARIOUS SOURCES

63. Protein the Most Prominent Organic Component of the Body.—The most prominent component of the body tissues, the skeleton excepted, is protein. This substance is the basis of the muscles and glandular tissues, and overshadows all other organic compounds in relative abundance. Liebig believed that a muscle does mechanical work at the expense of energy stored in it in the form of protein. The energy was supposed to come from the change of the complex protein molecule into simpler products, analogous to the change of complex molecules of wood into carbon dioxid and water during combustion, the energy set free being capable of appearing in part in the form of work.

If this view were correct, the amount of protein which is broken down daily should be profoundly influenced by the amount of work performed. Modern investigations have, however, established that work is ordinarily performed at the expense of the energy of carbohydrates such as starch and sugars taken in the food, or from fat. This was first shown by Pettenkofer and Voit (1) in 1866. These investigators observed that even a fasting man showed no increased protein destruction as measured by the amount of nitrogen eliminated in the form of waste end-products in the urine. Instead of prodigally wasting his muscle substance (protein) he burned fat as a source of energy. Recent investigations have proven that *following severe work* there is an increased elimination of nitrogen (1).

For many years physiologists assumed that the tissues of the human or animal organism were not capable of synthetic transformations so as to give rise to the formation of complex organic compounds from simple ones. The building up of organic substances from inorganic compounds was believed to occur only in plants during growth. The logical inference was that the wear quota of the protein-rich tissues must be replaced by new proteins from the food. Early observations on fasting men and animals established the fact that even during periods of ab-

stenance from food, tissue waste still goes on, and in the absence of protein in the diet the muscles and other tissues are used up. During a subsequent period of feeding, the lost muscle substance may be completely restored. One of the problems which early occurred to the inquiring mind of Carl Voit of Munich (2) was that of determining the amount of protein in the form of meat, which would suffice to prevent a nitrogen (protein) deficit in dogs. He did not actually determine the minimum amount of protein necessary to accomplish this, but instead, showed that with moderately large intakes of meat protein, the nitrogen which appeared in the urine as waste products of metabolism, plus that eliminated in the feces, was equal to that ingested in the food. In other words the body was in nitrogen (or protein) equilibrium.

64. **Gelatin is an "Incomplete" Protein.**—Gelatin, which results from incipient hydrolysis of connective tissue and the organic matrix of bone, is a protein of peculiar nature which early came to the attention of chemists. Gelatin and the casein of milk were among the proteins first to be separated in a state of approximate purity. Voit attempted to substitute with gelatin a part or all of the meat protein in the diets of his dogs and discovered that gelatin alone as the sole source of nitrogen could not prevent loss of body protein. There was something lacking in its makeup which made it an incomplete food. Gelatin became, therefore, a substance of unique interest to physiological chemists.

In 1849 Millon (3) discovered a reagent which when added to most proteins gives a characteristic brick red color. Gelatin does not exhibit this property. In 1879 Nasse (4) demonstrated that the reaction of Millon is due to the presence in the protein molecule of the amino-acid tyrosin, which is one of the digestion products of many proteins. Gelatin, therefore, does not yield tyrosin when digested. It has still other deficiencies which were later discovered. Tryptophan and the sulphur-containing amino-acid, cystin, are both lacking in its molecule. Gelatin has, therefore, long been known to be an "abnormal" or incomplete protein, and its value in nutrition has been the subject of many investigations.

Örum (5) and Munk (6) confirmed the earlier observations that a part of the protein could be substituted by gelatin, but that when it forms the sole source of nitrogen there is always a deficit.

Kossel discovered the chemical nature of the protein molecule to be a chain-like structure consisting of a number of amino-acids linked together, the amino group of one being united to the carboxyl group of its neighbor in the chain through abstraction of the elements of water. Digestion consists of the addition of the elements of water and the dissolution of the union. The correctness of this view was proven by Curtius and by E. Fischer, through synthesis, under the guidance of Kossel's theory (7).

65. **Principal Objectives in Researches on Protein in Nutrition.**—Researches in the field of protein nutrition during the last twenty-five years have had as their main objectives the solution of the following problems: 1. The digestibility of the proteins; 2. the number and nature of the amino-acids contained in proteins of plant and animal origin; 3. the amounts of each of these yielded by different proteins; 4. the extent of the digestive decomposition of proteins in the alimentary tract; 5. the ability or inability of the tissues to synthesize the various digestion products of proteins; 6. the immediate disposition of the products of protein digestion after absorption; 7. the chemical changes which take place during the catabolism or destruction of the amino-acids in the body; 8. the capacity of the body to synthesize protein when the requisite amino-acids are supplied in the food; 9. the determination of the relative efficiency possible in the transformation for purposes of growth of (a) individual proteins and of (b) the mixture of proteins in individual food-stuffs, into body proteins; 10. a comparison of the number and kinds of amino-acids required in the process of repair of tissue waste, an essential result of life activities with those required in the formation of new tissues for growth; 11. the physiological effects of nutrition with protein intake at different planes, or the discovery of the amount of protein from stated sources which serves to maintain the body in optimal nutritive condition.

It is not within the scope of this book to discuss all phases of this subject. An arbitrary selection of topics will be made, and only the last four problems will be considered. This is desirable because the literature relating to research along these lines is especially in need of being summarized and interpreted.

66. **Body Can Build Proteins from Simple Products of Digestion.**—The problem concerning the ability of the tissues to take a mixture of amino-acids and combine them into proteins for incorporation into living protoplasm, has been studied most adequately by Abderhalden (8). In one of his most suc-

cessful experiments a dog was fed during 100 days upon meat which had been digested to the amino-acid stage (erepton) by the successive action of pepsin, trypsin and erepsin, the protein-digesting enzymes of the stomach, pancreas and intestine, respectively. The digested meat was supplemented with non-nitrogenous nutrients. The animal remained in good health and gained 9.35 kg. in weight. It was demonstrated by such experiments that protein synthesis is possible when the diet furnishes all the essential amino-acids which serve as structural units in the formation of tissue proteins.

67. **Gelatin Is of Value When Supplemented with Certain Amino-Acids.**—Kaufmann (9) conducted the first experiment of a type which has been greatly extended by others. He fed dogs on diets in which gelatin was supplemented with tyrosin, cystin and tryptophan to the extent of 4.2 and 1 per cent respectively of the total nitrogen of the diet, the remainder being supplied by gelatin. It was found possible with this mixture to replace fully the protein lost through metabolism. These results he confirmed by experiments on himself. In 1905, when his investigations were made, no one suspected the necessity of including in the diet the three unidentified dietary factors fat-soluble A, water-soluble B and water-soluble C, which are concerned with the prevention of the development of a type of ophthalmia, polyneuritis and scurvy, respectively. His experiments were apparently so short that these omissions in the diet did not seriously interfere with the outcome of the study.

Abderhalden (8) sought to remove certain amino-acids from completely digested proteins. By means of feeding experiments with the protein digestion mixtures rendered incomplete, in that one or more of the complexes contained in tissue proteins were lacking, he sought to determine which, if any, of the digestion products are indispensable in the diet. The object was to determine whether, in certain cases, it is possible for the body to convert one amino-acid into another, that is, to synthesize a missing essential complex. He was able to remove practically all of both tyrosin and tryptophan from his digestion mixtures. The former of these is a cyclic compound and the latter a still more complex substance containing two types of cyclic structures in its molecule. Abderhalden demonstrated that these two amino-acids must be furnished in the diet if satisfactory nutrition is to be attained.

Henrique and Hansen (10) published similar studies which

led them to believe that the three diamino-acids, arginin, histidin and lysin, are not necessary in the nutrition of the rat. Their experiment consisted in keeping a record of the nitrogen intake and output of a rat during a period of 23 days while the animal was restricted to a diet containing only digested protein from which these three digestion products had been removed. It is very difficult to avoid loss of a part of the nitrogen of the urine in experiments with such a small animal, and it seems probable that their work was not free from error, since their results are at variance with those of other investigators. They may possibly have failed to remove completely from their protein the amino-acids in question.

68. **The Experiments of Willcock and Hopkins.**—Willcock and Hopkins (11) made a study of the incomplete protein, zein, the principal protein of maize, which was comparable with Kaufmann's studies with gelatin. Zein is entirely lacking in both lysin and tryptophan. These authors fed to young mice diets of purified food substances, in which zein was the sole source of protein (amino-acids), and observed that the animals died in less than 14 days in a state of torpor. When tryptophan was added to the food they lived about twice as long and remained lively until shortly before death. The addition of tyrosin did not improve the diet.

Willcock and Hopkins suggested that tryptophan may serve a two-fold function. It is an essential structural unit of the protein molecules of which the tissues are formed, and is perhaps a precursor of a substance which certain tissues elaborate. This, they suggested, is in the nature of a hormone or regulator of metabolism, without which death would supervene sooner than through specific starvation for protein alone.

69. **Final Proof of Protein Synthesis.**—Folin and Denis (12), Van Slyke and Meyer (13), and Davis and Whipple (14) have shown beyond a doubt that protein is readily synthesized from amino-acids, for in the intestine, the protein is digested to the amino-acid stage, and the identity of the food proteins is lost. In the process of growth, in the regeneration of liver tissue destroyed as the result of chloroform narcosis, or in the replacement of the complexes in the tissues lost through the disintegration of certain structures in normal metabolism of protoplasm the amino-acids derived from food protein are used for the construction of new proteins of structures different from those of the food.

Mitchell (15) conducted experiments with mice fed a diet mod-

elled after one which was extensively employed by Osborne and Mendel, and which will be discussed later. In this diet he replaced the protein by a definite mixture of amino-acids. The diet contained a product known as "protein-free milk," which furnished approximately half a maintenance ration of protein, but this fact was not known at the time. The efforts to keep mice alive on this diet containing from eight to fifteen amino-acids were unsuccessful. This was in part due to the failure of the animals to eat a sufficient amount of the food to meet their energy requirements. It was found necessary to feed the mice on alternate days on the portion of the food mixture minus the amino-acids, to induce them to take a greater amount of food. He found the omission of tryptophan of greater significance than that of other amino-acids.

70. **Does Growth Necessitate Amino-Acids in the Diet Not Essential for Maintenance?**—Geiling (16) digested casein of milk to the amino-acid stage and then precipitated the arginin, histidin and lysin with phosphotungstic acid as Henrique and Hansen (10) had done, and conducted experiments in feeding the portion of the protein without these diamino-acids. Mice were used as experimental animals. His diets also contained "protein-free milk," which, as will be shown later, contained protein nitrogen (amino-acids) sufficient to vitiate in great measure the results of his experiments. Geiling interpreted his findings as indicating that arginin and histidin are interconvertible in the body. He also concluded that lysin is not necessary for maintenance without growth. These observations were confirmatory of studies made by Ackroyd and Hopkins (17) and by Osborne and Mendel (18).

71. **The Transmutability of Certain Amino-Acids into Each Other.**—Ackroyd and Hopkins (17) had carried out feeding experiments with mice fed the essential non-nitrogenous nutrients supplemented with simple mixtures of purified amino-acids. Their conclusion was that if arginin is present in the diet histidin may be omitted, and vice versa. A similar relationship they found between tyrosin and phenylalanin, the structural formulas of which are closely similar. This was the first instance where it was believed that it had been demonstrated that one amino-acid may be converted into another.

72. **Endogenous and Exogenous Metabolism.**—In 1905 Folin (19) published three remarkable papers in which he made it clear that the process of the destruction of the greater part of the protein which is digested and absorbed daily, and of its

conversion into the waste products which constitute the normal components of the urine, differs markedly from that type which is involved in the normal functioning of the tissues of the living body. The end-product of the first type is principally urea, while creatinin and uric acid are prominent components of the latter. When a diet free from protein or other nitrogenous compounds is taken in amount sufficient to cover the energy requirements of the body, the urine will, after a few days, contain about 60 per cent of its total nitrogen in the form of urea, 18 per cent as creatinin, 7.0 per cent as ammonia, and 3.4 per cent as uric acid. The remainder, which will amount to about 12-14 per cent of the total, is in forms which are in great measure uncharacterized, and which cannot as yet be estimated individually. A urine having this composition represents what Folin termed endogenous metabolism, to distinguish it from exogenous metabolism, which is concerned with the destruction of food protein that has never become a part of the living protoplasm of the body. The magnitude of the endogenous process is surprisingly constant, whereas that of the latter is very variable, and is determined by the consumption of protein. On ordinary planes of nutrition, exogenous metabolism or destruction of food is superimposed upon the endogenous or tissue waste type and the composition of the urine gives a composite picture of the two.

73. **An Attempt to Differentiate Between Nutritional Requirements for "Repair" Versus Growth.**—McCollum (20) attempted to utilize Folin's discovery as a means of studying the problem whether an amino-acid supply which is inadequate for the support of growth, would be satisfactory for maintenance. A farm pig was given a nitrogen free diet of starch, salts and water until the exogenous metabolism disappeared, as shown by the composition of the urine. In a subsequent period a definite amount of an incomplete protein such as gelatin or zein was to be added to the experimental diet of carbohydrate, salts and water. From the increase in the nitrogen output in the urine and from the change in the forms in which it appeared, it was believed to be possible to decide to what extent, if at all, the amino-acids of the incomplete protein were utilized.

It was found that young swine, which were used as experimental animals, readily ate a sufficient amount of the nitrogen free diet to cover their energy requirements, and could easily be brought into the condition, in which they exhibited only the endogenous type of metabolism. When to pigs in this condi-

tion, a known amount of nitrogen in the form of urea, an end product of metabolism, was added to the diet it was all recovered in the urine *in addition to the amount derived from endogenous sources.* The percentage composition of the urine with respect to creatinin and urea showed the expected alterations the former representing less and the latter more of the total nitrogen of the urine.

When, instead of urea, gelatin or zein was administered in quantities sufficient to supply exactly the amount of nitrogen derived from endogenous metabolism, *the nitrogen from these "incomplete" proteins was only in part excreted in the urine in addition to the amount derived from endogenous sources.* The results showed that 60 per cent of the nitrogen of gelatin was excreted and 40 per cent retained for some purpose in the tissues, presumably for the partial repair of tissue waste. Under the same experimental conditions 73 per cent of the nitrogen of zein was retained and 27 per cent excreted in addition to the amount expected from endogenous sources.

74. **Experiments on the Synthesis of Amino-Acids from Ammonia.**—Almost simultaneously Grafe (21) announced that nitrogen equilibrium could be attained on a diet of carbohydrate and ammonium acetate. Abderhalden (22) repeated this work and found a partial utilization of ammonium salts for replacing the nitrogen lost through tissue waste, but denied the possibility of attaining nitrogen equilibrium. Underhill and Goldschmidt (23) confirmed the view that there is under these conditions a sparing action of body protein by ammonium citrate, but all the tissue loss could not be replaced from nitrogen in the form of ammonium salts. In all these studies we now know that the diets employed were deficient in the three vitamins, fat-soluble A, water-soluble B, and water-soluble C, so the interpretation of the results are not now as satisfactory as they once appeared to be.

It has been abundantly demonstrated by several workers, that the simplest of the amino-acids, glycocoll, is readily synthesized by the body tissues (24). Casein contains no glycocoll, yet it is a complete protein, and can meet all the requirements of an animal for nitrogen in the form of amino-acids. From these results it is safe to conclude that the tissues of the higher animals are capable of synthesizing certain amino-acids, and that these are made use of in some way to conserve the body proteins, even though the list which can be so synthesized is incomplete. It

appears certain that tyrosin, tryptophan, and probably all the other cyclic amino-acids and cystin cannot be synthesized by the mammal (25). Abderhalden suggested that the sparing action of ammonium salts is due to prevention of destruction of some of the amino-acids derived from the tissues, and that these may be used over again.

75. **Attempts to Prove the Superiority of Proteins of One's Own Species over Foreign Proteins in Nutrition.**—Michaud (26) sought to verify with experiments on dogs, the theory that the more similar the food proteins to those of the tissues which they are destined to form in the body, the higher would be their biological value as nutrients. He allowed dogs to fast for a time to reduce their nitrogen output to the minimum of tissue destruction. He then fed them a non-nitrogenous diet supplemented with various amounts of protein from different sources. His findings lead us to the belief that the proteins of the same species of animal are superior in dietary value to proteins obtained from another species or from plants. Dog muscle and dog serum proteins were of higher nutritive worth for the dog than muscle or serum proteins from the horse. A mixture of dog tissues (muscle, blood and glandular organs) was also superior to any of the other proteins studied. Gliadin and edestin, proteins from the wheat kernel and hempseed respectively, were of the lowest value. We now know that his diets were by no means comparable in their quality with respect to factors other than protein. All except those in which the glandular organs were included were very deficient in the anti-neuritic, anti-ophthalmic and anti-scorbutic substances, as well as very poor in their mineral content. It is not possible, therefore, to accept without doubt his interpretation of his results.

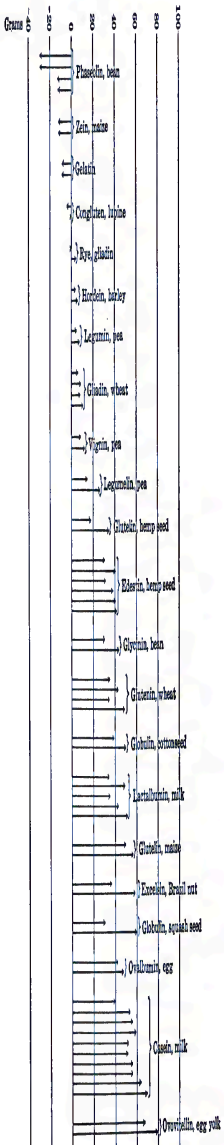
76. **Comparative Nutritive Values of Individual Proteins.**—During the past decade numerous experiments have been conducted with a view to determining the relative nutritive values of a large number of individual proteins. The proteins studied were in the greater number of instances those which are the easiest to prepare in quantity in a state of purity from substances of animal or vegetable origin. The most prominent investigators who have pursued this line of inquiry are Osborne of the Connecticut Agricultural Station and Mendel of Yale University.

It has been pointed out in Chapter II that these investigators first sought to make comparative studies of isolated proteins by adding them to a mixture of purified carbohydrates, fats, mineral

salts and water, and invariably met with failure, for in every instance the animals suffered steady decline. After their failure with the diet composed entirely of purified food substances, every component of which was known, they began a series of studies with what they believed to be essentially the equivalent of a purified food mixture. This involved the inclusion in the diet of about 28 per cent of a product which they called "protein-free milk." On several occasions it was pointed out by McCollum that the properties of this product were such as to seriously impair their results (27). Osborne and Mendel apparently thought that this criticism was not well founded, for they continued to employ "protein-free milk" in almost all of their work during a period of seven years, and without successfully justifying its use. They finally abandoned the use of the product in 1917, at which time they adopted essentially the method of study which had been described by McCollum and Davis in 1915 (28).

77. **Osborne and Mendel's Studies on Protein Metabolism.**—There were three principal phases of protein nutrition which Osborne and Mendel discussed in the light of their data. The importance of their deductions is so great and the defects in their method so difficult for the inexperienced to appreciate, that a somewhat full discussion is warranted of the manner in which "protein-free milk" vitiated a considerable part of a research of a most comprehensive type. Three phases of protein metabolism will be discussed here: The comparative values of the individual proteins in growth; the protein requirements of the animal body in maintenance as contrasted with growth; the possibility of the existence for the maintenance of the species of a synthetic capacity in the maternal organism, through the medium of the placenta and of the mammary gland, which cannot be affected by other body tissues for the maintenance of the life of the individual. These will be considered in the order enumerated.

78. **Methods of Comparing the Biological Values of Individual Proteins.**—One method which they employed to illustrate the striking differences in the values of the proteins from different sources for the support of growth, was that of feeding a series of groups of animals on a diet of constant composition, but with a different protein, carefully isolated and purified, as a component in the diet of each experimental group. The amount of growth or of loss in body weight of the animals during the first thirty days on the experimental diets was recorded and made



The above table is slightly modified from a publication by Osborne and Mendel, Zeit. f. physiol. Chem., 1912, lxxx, 307.

the basis of comparison. The diet consisted of the following substances:

Purified protein	18.0 per cent
"Protein-free milk"	28.2 " "
Starch	20.8 " "
Agar-agar	5.0 " "
Fat	28.0 " "

The results obtained with a series of proteins are shown in graphic form in the diagram on page 68.

An inspection of this table shows that animals restricted to bean protein lost weight rapidly. Those fed zein, the principal protein of the maize kernel, and also those fed gelatin lost weight, but not so rapidly. Conglutin, a protein from the lupine, and gliadin of rye, served to maintain weight without growth, and little growth was secured with hordein of barley or legumin of pea. All the other proteins listed were capable of promoting growth when fed with the other substances in the diet.

A second method which Osborne and Mendel employed for the comparison of the biological values of different proteins for growth in the rat, was to observe the rapidity of growth of the animals when fed diets of the type described above, in which but a single protein was added, the character of the protein varying in different experiments (30). A third method was to carefully establish the amount of increase in body weight which was possible as the result of the consumption of a definite amount of protein, the nature of the remainder of the food mixture remaining essentially constant throughout the series of experiments (31). As an illustration of the results secured by the latter method the following table is representative:

Rat	Diet	Initial body weight	Gain		Intake of	
					Total food	Protein
		grams	grams	days	grams	grams
2115	9% lactalbumin.........	65	99	80	589	43.7
2123	" "	43	89	80	395	29.3
2207	" "	59	91	80	575	42.6
2210	" "	60	93	80	560	41.5
2051	9% casein (cow's milk).	42	59	80	435	35.2
2110	9% edestin (hemp seed)	52	60	80	465	38.9
2044	4½% lactalbumin (milk)	42	44	80	371	13.8
2049	4½% lactalbumin.......	41	54	80	454	16.8
2118	4½% casein............	59	-3	80	366	14.8
2113	4½% edestin...........	83	14	80	459	19.2
2114	4½% casein............	65	29	80	464	19.4

It will be observed that rats which ate similar amounts of food grew much faster on 9 per cent of lactalbumin than on casein or edestin. Similar differences were observed when the lower protein intake was fed. At the time these experiments were carried out it was believed by Osborne and Mendel that they actually represented quantitative comparisons of the values of these proteins for growth. It will be apparent from data discussed later in this chapter in connection with the nutritive value of gliadin, that lactalbumin as the sole source of protein cannot support any growth whatever. Its excellent showing in the above experiments was due to the supplementary action of the amino-acids contained in the "protein-free milk" which was fed with it.

79. **"Protein-Free Milk" a Disturbing Factor in These Experiments.**—Since the nitrogen contained in "protein-free milk" can act as a source of certain amino-acids, it is obvious that the true dietary value of any series of proteins which it is desired to compare cannot be secured, when they are studied by the method involving the concomitant feeding of this material. The scope of the studies of Osborne and Mendel, and the importance of the deductions which have been drawn from them are so great that a detailed exposition of the action of the nitrogenous constituents of "protein-free milk" in vitiating their results will be presented. This is best brought out by their studies of the nutritive value of gliadin, one of the principal proteins of the wheat kernel. These are of fundamental importance because their interpretation involves the question, not only of the biological value of "protein-free milk" as a source of amino-acids, and its bearing on the recorded nutritive significance of numerous proteins, but likewise on the problem whether the processes of maintenance without growth, or the repair of tissue waste, is of a lower order than those of growth requiring fewer amino-acids than the latter.

80. **Properties of Protein-Free Milk.**—"Protein-free milk" was prepared by acidifying with acetic acid, milk which had been freed from fat by centrifuging. The resulting whey, after the removal of the casein which flocks out on the addition of acid, was next heated to boiling to coagulate the lactalbumin. These are the principal proteins of milk, and with their removal about 93 per cent of the total nitrogen contained in the milk is abstracted. The solution which was filtered free from lactalbumin was evaporated to dryness, leaving a yellowish residue consisting of milk sugar, most of the salts of the milk, and a

certain amount of nitrogenous compounds for the separation of which no method is known.

Osborne and Mendel held the view, which their own studies finally showed to be untenable (32), that the amount of protein or its equivalent, resulting from the digestion of milk protein or directly secreted by the mammary gland, which was contained in their "protein-free milk" was too small to be a factor of significance in their experiments. The final product they included in their diets contained about 0.7 per cent of nitrogen (30), which would be equivalent, if it were all in the form of protein or of its digestion products, to 4.37 per cent of dry matter. It is well known that some urea, purins, creatin, and other simple nitrogenous substances which circulate in the blood are always found in milk. It is certain, however, that there is a considerable amount of nitrogen in "protein-free milk" in forms yielding amino-acids in the body. Its property of enhancing certain incomplete proteins makes this view imperative.

From what has been said in Chapter II it will be clear that a protein which is of low biological value for growth because of the fact that one or more of the digestion products which it contains is present in too small an amount to make possible its efficient transformation into body proteins, may be greatly enhanced in growth promoting value by the addition of the missing amino-acid or acids. This has been illustrated in the case of gelatin and for the meat digests prepared by Abderhalden (p. 61). It will be readily understood, therefore, that when a series of purified proteins was fed to young animals, the remainder of the diet consisting of 28 per cent of "protein-free milk," together with non-nitrogenous nutrients similar to the following:

Protein	18.0 per cent.
"Protein-free milk"	28.2 " "
Starch	20.8 " "
Agar-agar	5.0 " "
Fat	28.0 " "

the amino-acids furnished by the "protein-free milk" may improve the quality of some or all of the pure proteins, and so change the experimental results as to make it unwarrantable to draw any conclusions concerning their relative nutritive values when fed without such an amino-acid supplement.

81. **Milk Contains Protein-Digesting Enzymes.**—Babcock and Russell (33) and Freudenreich (34) demonstrated in milk

the presence of protein digesting enzymes. The bacteria found in all market milks are in many instances capable of digesting proteins. There is, therefore, abundant opportunity for milk used for the preparation of "protein-free milk" after it has been kept for an interval of 24 hours or more to contain partial digestion products of protein that would not be removable by acidifying or by coagulating. All such compounds would remain in the final product.

Osborne and Mendel felt justified by the work of Munk (35) in assuming that the 0.7 per cent of nitrogen in "protein-free milk" was not a disturbing factor in their experimental studies. Munk had, twenty years previously, sought by coagulation and by precipitation with various reagents, to determine the amount of "non-protein" nitrogen in milk (36). He arrived at the conclusion that one-fifteenth of the total nitrogen in milk is in forms other than protein. Osborne and Mendel accepted this figure as correct and reasoned as follows: A certain amount of milk contains a known amount of nitrogen, a part of which is in the form of proteins and can be removed by the methods employed. On evaporating the resulting whey to dryness the "protein-free milk" which remains contains 0.7 per cent of nitrogen in forms not known. From the weight of "protein-free milk" obtained, the total nitrogen it contained was calculated. From this amount they subtracted one-fifteenth of the total nitrogen contained in the milk with which they started. The remainder was assumed to represent "protein," or nitrogen having a nutritive value. There is no evidence in Munk's data, or in any furnished by Osborne and Mendel to show that the one-fifteenth of the total nitrogen of milk, which remained after the removal of the casein and lactalbumin, and which was disposed of by mathematical treatment of their analytical data, was not a source of amino-acids, and capable, therefore, of enhancing the nutritive value of poor proteins making them appear to have higher biological values than they possessed.

A diet such as was used in their studies, and which contained 18 per cent of added protein in purified form, together with 28 per cent of "protein-free milk," would derive 93 per cent of its total nitrogen from the former and 7 per cent from the latter source. The biological evidence is conclusive that this 7 per cent of the nitrogen of their diets supplemented certain proteins with which it was fed, in a very effective manner and led to entirely erroneous conclusions. This is well illustrated by the way

in which it supplements gliadin, one of the principal proteins of wheat, and lactalbumin of milk.

82. Are Fewer Amino-Acids Essential for Maintenance Than Are Required for Growth?—In 1912 Osborne and Mendel (37) performed an experiment which they interpreted as demonstrating the processes of maintenance as being of a lower order than those of growth, and that repair of tissue waste can be effected without the amino-acid lysin, whereas this complex is indispensable for growth. There were two confusing factors in this experiment, the "protein-free milk" nitrogen, and the erroneous belief that gliadin contained but very little lysin.

Osborne had carefully determined the amounts of lysin in numerous proteins and had found the content of this substance in gliadin to be 0.15 per cent. This amount is extremely small compared with the yields obtainable from many other proteins, notably those of animal tissues. This is illustrated by the following table (38):

LYSIN IN PROTEINS

Lactalbumin	8.10 per cent.	Glutelin (maize)	2.93 per cent.
Halibut muscle	7.45	Glutenin (wheat)	1.92
Ox muscle	7.59	Edestin (hemp seed)	1.65
Casein (cow's milk)	7.61	Amandin (almond)	0.72
Vitellin (egg yolk)	4.81	Gliadin (wheat)	0.16
Albumin (hen's egg)	3.76	Hordein (barley)	0.00
Legumin (pea)	4.98	Zein (maize)	0.00
Phaseolin (Kidney bean)	4.58		

In the experiment just referred to they restricted young rats to a diet consisting of gliadin 18.0, "protein-free milk" 28.2, starch 20.8, agar-agar 5.0 and lard 28.0 per cent. The animals were able to maintain their weight during periods as long as 500 days, but were unable to grow to any appreciable extent. When lysin, one of the eighteen digestion products of nearly all proteins, was added to the diet to the extent of 3 per cent of the protein content, the animals were capable of normal development.

At the time these experiments were conducted with gliadin it was assumed that this protein contained but 0.16 per cent of lysin. However, Osborne, Van Slyke, Leavenworth and Vinograd (39) in 1915 made new analyses of gliadin and other proteins, by a more satisfactory method than that which Osborne had earlier employed (40). They found that gliadin contains

about 1.21 per cent of lysin, or about seven times what it was assumed to contain at the time when the conclusion was drawn from feeding experiments with this protein, that lysin is not necessary for maintenance without growth. With this knowledge available, and with the fact made evident that the nitrogen of "protein-free milk" in the quantities used in their experiments, amounts to about half the maintenance requirement of a young animal, there is no longer any reason to regard these data as having any bearing on the problem of the possible dissimilarity in the amino-acid requirements for the processes of maintenance as contrasted with those of growth.

83. **Is the Mammary Gland Able to Synthesize the Amino-Acid Lysin?**—The observation that a female rat which had been restricted during 178 days to a diet containing gliadin and "protein-free milk," was able to become pregnant and produce four young and to suckle these to the age of 23 days, was also presented as evidence that maintenance or the development of young in the uterus, and the formation of milk with which to nourish the young following their birth, are possible on a diet lacking in lysin and incapable of supporting growth. From what has been said previously as to the actual content of lysin in gliadin and the nutritive value of the nitrogen of "protein-free milk" it will be appreciated that the data tend rather to support the view that no differentiation can be made of the nutritive needs of an animal during growth as contrasted with an adult drawing sustenance for the performance of the functions of reproduction and the rearing of young. This mother was simply being nourished on the lowest intake of lysin possible for her requirements under the experimental conditions.

84. **The Amino-Acid Lysin Is the Limiting Factor Determining the Value of Certain Proteins.**—There is no room to doubt that lysin is the limiting factor in this diet, but gliadin furnished decidedly more of this amino-acid than was at the time supposed. Some indication of the nutritive value of the nitrogenous compounds of "protein-free milk" is afforded by experiments carried out by McCollum and Davis (27). They showed that young rats slowly lose weight when confined to a diet in which the entire protein content limited to 1.5 per cent of the food mixture, was derived entirely from skim milk powder. The young rats, however, maintain weight over considerable periods when the amount of milk proteins is increased to 3 per cent of the food mixture. On the other hand, 1.5 per cent of milk pro-

tein supplemented with nitrogen equivalent to 1.5 per cent of protein derived from "protein-free milk" served to maintain the animals approximately as well as did 3 per cent from milk powder. From this observation they drew the conclusion that the nitrogen in "protein-free milk" has approximately the same nutritive value as that contained in milk proteins. This would not necessarily be true when it serves as the sole source of nitrogen in the diet, but it is when this product is combined with the proteins of milk in equivalent amount.

85. The Residual Nitrogen of Protein-Free Milk Can Supplement Certain Incomplete Proteins.—The most striking illustration of the value of the nitrogen of "protein-free milk" as a source of amino-acids is seen in its supplementary relation to lactalbumin. The comparative values of casein, edestin and lactalbumin when fed supplemented with this product are shown on page 69. These indicated that lactalbumin was far superior to either of the other proteins for growth. A similar result was observed in experiments designed to show the smallest intake of each of these proteins which would just serve to maintain young rats in weight equilibrium (41). In these experiments diets were employed, having a composition similar to that described in connection with the gliadin studies and containing 28 per cent of "protein-free milk." In some instances, however, but 2 per cent of purified protein were added to the food mixture. In such cases the nitrogen of the purified protein amounted to only 37 per cent of the total, the remaining 63 per cent being derived from the "protein-free milk." In the interpretation of the results no account was taken of this latter increment. Under these experimental conditions lactalbumin appeared to be a protein of extraordinary value.

86. Lactalbumin an Incomplete Protein.—McCollum, Simmonds and Parsons (42) restricted young rats to a diet which contained lactalbumin as the sole source of nitrogen and could not secure any growth, even with 18 per cent of protein in the diet. They drew the obvious conclusion that since the same diet was complete when casein replaced the lactalbumin, the latter must be a poorly constituted protein. This has been confirmed by Emmett and Luros (43). A later experience of Osborne and Mendel (32) convinced them also that lactalbumin was lacking in some constituent which is essential in proteins of the "complete" type. They found a diet consisting of purified food substances, including 18 per cent of lactalbumin, inadequate

for the support of growth even when small additions of yeast proteins were present in the diet. Yeast proteins do not appear to supplement lactalbumin, whereas the small amount of nitrogenous substances in "protein-free milk" are very effective for this purpose. In this connection Osborne and Mendel state "For some as yet unknown reason the majority of the rats grew normally (on the diets containing "artificial protein-free milk," butter fat, starch, lard and yeast)* when the protein used was casein, whereas they have usually failed when it was edestin, and almost invariably when lactalbumin, cottonseed globulin, cottonseed proteins, or squash seed globulin was fed. This result surprised us because all of these proteins had earlier led to normal growth when used in rations containing natural "protein-free milk." The failure to grow on the "artificial protein-free milk"-yeast was especially unexpected in the case of lactalbumin for our former experience had demonstrated that even exceptionally small amounts of this protein promoted normal growth." It is certain that any experiments directed toward making a quantitative comparison of the nutritive values of isolated proteins, have in them a disturbing factor wherever "protein-free milk" was employed.

87. **The Nitrogen of Protein-Free Milk Is in Part in the Form of Amino-Acids.**—Chemical studies which contribute to our knowledge of the nature of the nitrogenous constituents of "protein-free milk" have been made by Osborne and Wakeman (44), Denis and Minot (45) and Kennedy (46).

It should not be inferred from the above critical review of the rôle played by "protein-free milk" in their experiments, that the numerous studies conducted by Osborne and Mendel, in which this product was used, are without significance. Quite the reverse is true. They serve admirably to emphasize the variations which exist in the nutritive values of proteins from different sources. They leave no room for doubt that in a number of proteins from vegetable sources lysin is the limiting factor which determines their value for growth. They demonstrate that the sulphur-containing amino-acid, cystin, is the limiting factor in casein, and that the supplements which are essential in order to render zein nutritively complete are lysin and tryptophane. Even when these are added, however, and the protein is made adequate for growth, it is still further improved by the addition of the diamino-acid, arginin. They established the principle that the nutritive

*Parenthetical expression the author's.

value of a protein depends upon the quality and quantity of the amino-acids which it yields. Their studies failed, because of the use of the protein-free milk, to yield any quantitative comparisons of the biological values of different proteins. But extensive as were the studies discussed in this chapter, they form but an incident in the scientific work of these distinguished investigators.

The effects of "protein-free milk" in influencing the outcome of numerous experiments has been dealt with somewhat at length because, although Osborne and Mendel have themselves furnished data which clearly indicate the part which this substance played in their work, the observations were never definitely correlated with their earlier work, so as to make clear their changed views. For the constantly increasing number of students in this field it seemed desirable to offer this digest of one phase of the literature in order to show the true status of our knowledge in this field.

88. Feces of Normally Fed Rats Served to Complete a Diet of Purified Food Substances.—In some of these early experiments with purified food-stuffs, Osborne and Mendel (46) added about one gram per week's ration of dry feces of normally fed rats to their experimental diets. Animals which were rapidly declining on the diets of purified casein, carbohydrate, fat (lard) and a salt mixture, were markedly benefited by the addition of one per cent or thereabouts of feces of normal rats to their diet. Some were able to grow for a time and the decline of all was checked by this addition. To explain this beneficial effect of the inclusion of feces in the diet, several possibilities were suggested and discussed. One was the possibility that the bacteria thus introduced into the alimentary tract were able to elaborate substances (e. g., amino-acids) necessary to complete the defects in the purified protein contained in the diet. This seemed inadequate, because with other purified proteins serving as the sole source of amino-acids, the inclusion of feces did not render the diets complete. It is possible that the body cannot thrive unless the alimentary tract harbors a flora of certain types of micro-organisms. This is a very difficult point to establish, and indeed, has not been finally settled. There was also the possibility that the small amount of protein introduced into the ration with the fecal bacteria might be sufficient to supplement the deficiencies of the protein of the diet.

In the light of later developments it appears that the rats which were confined to a diet of purified casein and otherwise

of purified food substances, were benefited primarily by the inclusion of both fat-soluble A and water-soluble B, which the feces of normal rats contained. This served to so far complete the diet that the animals were given a new lease of life.

89. **Stunting of Growth Through Inadequate Protein Does Not Result in Loss of Capacity to Grow.**—Osborne and Mendel fed young rats on diets which were fairly satisfactory in their composition with respect to all factors other than protein. Their content of protein was below the amount which would suffice for the support of growth. The animals restricted to such food supplies remained stunted for long periods and yet were able, when later the amount of protein in their diets were increased, to resume growth at rates which the experimenters regarded as faster than rats ordinarily grow on a "normal" diet. From these results the deduction was drawn that interruption of growth does not result in the loss of the capacity to grow (46).

This generalization is too sweeping. It is true that rats which are stunted by means of protein starvation retain for long periods their capacity to resume growth and of a fairly normal character, the form of the grown animal being more or less closely similar to that of animals whose growth to adult size has been uninterrupted. McCollum and Simmonds (46) have found that rats which are at an early age kept upon diets in which the inorganic content is unsatisfactory, develop abnormal forms, and become permanently stunted. They become stocky, owing to failure to grow in length. Such animals may grow to a slight extent if their diet is later made satisfactory, but they always remain deformed. Any nutritive regimen which will induce rickets will, they find, markedly interfere with subsequent growth, when later, the faults in the diet are corrected.

Animals, whose growth has been suspended by depriving them of fat-soluble A, or water-soluble B, are able to resume growth upon the inclusion of the missing complex in the diet. It is not possible, however, to carry animals on such diets for long periods, because of the disaster which inevitably befalls them.

90. **Correlation of Nutritive Value of Certain Proteins with Their Lysin Content.**—Following the studies which led Osborne and Mendel (37) to conclude that the amino-acid lysin is not necessary for maintenance but is indispensable for growth, Osborne, Van Slyke, Leavenworth and Vinograd (39) made a very careful analysis of the principal proteins of the endosperm of wheat, maize and rice kernels, and found them to yield 1.58,

0.97 and 4.26 per cent, respectively, of the amino-acid lysin. They correlated these results with those of Thomas (47) secured in brief experiments upon himself and stated: "It is rather striking that the figures for the utilizability of these proteins correspond so closely with the lysin which they yield." The three-day type of digestion trial employed by Thomas, in which the factor of growth is not concerned, can be scarcely regarded as affording data comparable with the standards required in present-day experimental work.

91. **Mistaken Views as to Unique Importance of Lysin.**— Buckner, Nollau and Kastle (48) interpreted Osborne and Mendel's data as showing that "lysin is primarily responsible for the stimulation of growth." They apparently regarded the planning of farm rations so as to insure a sufficient amount of this amino-acid, as one of the specific agricultural problems of practical importance. These investigators fed chicks such complex mixtures as wheat, wheat bran, sunflower seed, hemp seed and skim milk, and contrasted the growth and well-being of these chicks with others restricted to barley, rice, hominy, oats and gluten flour. The former were well nourished and grew in a normal manner while the latter were stunted and miserable-looking creatures. Buckner, Nollau and Kastle interpreted their results as being due to "differences in the amino-acid content of the two rations and in all probability to differences in the lysin content."

It will be observed that the poor ration used in the feeding of chicks was limited to cereal grains and their by-products. One of the most important generalizations that can be made as the result of modern nutrition investigations is that it is not possible to secure a diet composed entirely of seeds of plants which will promote good nutrition over any considerable period. The diet in question was, it is true, poor in the amino-acid lysin, but its mineral content was deficient in certain elements, notably calcium, phosphorus, sodium and chlorin, so that growth was prevented in their chicks, even if the proteins had been of better quality. Furthermore, this diet was very deficient in the substance fat-soluble A, without which prolonged well-being is not possible. It contained but a trace of the anti-scorbutic substance, which may have been of some importance in preventing the development of the chicks. The good diet on the other hand was composed in great part of whole seeds, the germ of which improved the quality of the entire mixture of vegetable components

to an important degree. The bran was important as a source of mineral salts, since the cortical layer of seeds is especially the region in which these occur in the seed. When in addition to these differences between the two diets, the presence of skim milk in the successful one is considered, it becomes apparent that the two diets were in no sense comparable even in regard to factors other than the lysin content. It can confidently be predicted that a liberal addition of lysin to their poor diet, or indeed, a liberal addition of all the essential digestion products of protein in the form of a purified protein such as casein, would not have changed the outcome of their experiment.

In a later study Osborne and Mendel (49) employed maize gluten, which contains about 1.0 per cent of lysin, supplemented with "protein-free milk" sufficient to furnish 1.33 per cent of the total nitrogen of the food mixture, as the source of protein for growing chicks. They compared the growth obtained with this protein mixture with that obtained with rations similar in their make-up except that the maize-gluten nitrogen and "protein-free milk" nitrogen was supplemented with lactalbumin or cottonseed flour. The latter supplements are known to be rich in lysin. The results were interpreted as confirming the conclusions of Buckner, Nollau and Kastle in respect to the effect of foods high and low in lysin on the growth of chicks.

From the standpoint of practical nutrition these experimental studies all tended to focus attention upon lysin as an amino-acid of more importance than other indispensable digestion products of proteins, because of the assumption that it is relatively less abundant in proteins of the cereal grains, as wheat, maize, and others.

92. Other Amino-Acids Than Lysin Are as Important as Limiting Factors in Protein Nutrition as Is Lysin.—This view is reflected in the publications of Johns and his co-workers (50), who have emphasized the importance of discovering among the vegetable foods sources of proteins rich in the basic amino-acids, arginin, histidin, and lysin, and especially the latter. The logic of such a view is apparent, and is amply justified by the known peculiarities of the cereal proteins which form so important a source of protein in the nutrition of man and animal. These peculiarities have been brought to light by the studies of Osborne and Mendel, who have shown that the cereal proteins are especially deficient in this group of protein-building units.

The view that any generalization regarding the cause of the low biological value of the proteins of any series of natural foods

is possible, is, however, without foundation. While lysin is the limiting factor in some proteins it appears not to be more frequently so than certain other amino-acids. While it is logical on theoretical grounds to combine a food which is known from the results of chemical studies to be low in lysin, or any other essential amino-acid with another food especially rich in such compound, it is not safe to place much confidence in the results of chemical analysis in this special field of inquiry. This is well illustrated by the deductions regarding the special importance of lysin in foods. McCollum, Simmonds and Pitz (51) have shown that, poor as are the proteins of the maize kernel in lysin, this is not the essential amino-acid which is present in smallest amount in proportion to the amount required for the formation of new tissues during growth. It is not the limiting factor in determining the value of the maize kernel proteins. It would not be out of place to describe the procedure which established these facts. A food mixture consisted of a single grain so supplemented with inorganic salts and butter fat as to be satisfactory for the promotion of growth and prolonged well-being, except that the protein was too low in amount to promote growth at the normal rate. In all cases the diets were shown to be made highly efficient for growth by the addition of a purified protein alone, when that protein was casein of milk. This is a complete protein for the nutrition of an animal. Rations of this type in which wheat, maize or oat kernel were employed, were fed to young rats, and the same rations supplemented with gelatin or zein were fed to other groups. Zein, the most abundant protein in maize, is entirely lacking in trytophane and lysin, whereas gelatin contains about 6 per cent of lysin.

Obviously, if lysin were the limiting amino-acid in each of these three grains, the addition of gelatin should enhance the value of the proteins in all cases and the nutrition of the animals should be correspondingly improved. The addition of zein, on the other hand, should not lead to improvement. The outcome of the experiments showed that zein does not supplement the proteins of the wheat or maize kernels, but does improve the proteins of the oat kernel in a fairly effective manner. Later investigations have caused McCollum and Simmonds to question these conclusions so far as the oat kernel is concerned. Lysin may possibly be the limiting factor in the oat kernel. Hogan found that the addition of lysin and tryptophane to maize did not enhance the nutritive value for growth of swine (52).

Gelatin supplements the proteins of both the wheat and oat

kernel in a very efficient manner, but does not enhance the value of maize kernel proteins. Since gelatin is rich in lysin, the latter amino-acid is not the limiting factor in the proteins of the maize. The improvement of diets containing maize gluten, which Osborne and Mendel (53) observed to follow the introduction of lactalbumin or cottonseed proteins, was not as the authors believed, the result of the addition of the amino-acid lysin.

Some further deductions are possible from these data. These support the view, but do not prove it adequately, that lysin is the limiting factor in wheat kernel proteins. Since gelatin contains no tryptophan or tyrosin and but a trace of cystin, it suggests that none of these three amino-acids are the ones present in minimal amounts in wheat or oat proteins.

93. **Lactalbumin, Although Very Rich in Lysin, Is an Incomplete Protein.**—A further illustration of the fact that no generalization can be made on the basis of available data, concerning the greater importance of lysin as a practical problem in nutrition, than certain other amino-acids, is afforded by the history of lactalbumin studies. These have already been described (p. 69). Although this protein is one of the richest known in lysin, it is an incomplete protein and not capable of supporting growth unless it is supplemented with a source of a certain missing complex or complexes, the identity of which has not been established.

The proteins of the pea or bean appear from chemical data available, to be more closely similar in their constitution to the principal animal-tissue proteins than are those of the cereal grains, and they are certainly more abundant sources of lysin. Their dietary values, when unsupplemented, fall far short, indeed, of those of the cereals.

Studies like those that have been described, in which the aim was to determine the possibility of supplying the needs of a growing animal for protein-building material with mixtures of amino-acids lacking in one or more of those found among the digestion products of most proteins are extremely valuable. So are studies directed toward determining the nature of the simple additions of amino-acids which make complete certain proteins themselves inadequate as a source of nutriment for tissue building. It is these types of investigations which bring to light the synthetic capacity of the cells and contribute to an understanding of the chemical processes normal to the living body (54). The problems concerned with making the best possible use of

our available food-stuffs demand, among other things, an accurate understanding of the biological value for the purposes of maintenance and growth, of the protein mixtures contained in our foods. These problems also demand a knowledge of the extent to which the various possible combinations of foods furnish protein mixtures superior to those of the individual foods when the latter constitute the sole source of protein in the diet (55).

94. **Several Other Dietary Factors as Important as Protein.**—The problem of practical nutrition is really much broader than this, for protein constitutes but a single factor of importance in nutrition. The content of the essential mineral elements in the diet, and of the several unidentified factors, the absence of which leads promptly in each case to the development of specific pathological conditions, are of equal importance from the standpoint of the well-being of the body. The discovery of the means of making the nice adjustments in a quantitative way among all the factors best adapted to promote optimum development and of the means of preserving the harmonious rhythm of the metabolic processes in the best possible manner, is the end sought by students of nutrition. The various factors mentioned will receive attention in later chapters.

95. **An Example of Faulty Technic in Earlier Experimental Studies on Nutritive Worth of Protein.**—McCollum sought to compare in growth value the proteins of wheat, maize and oat kernels in young swine. He confined the animals in metabolism cages, thus making possible the collection of the excreta during a period of thirty to sixty days, during which the animals were fed exclusively on a single grain and water (56). From the record of the nitrogen intake and output of the animals he calculated the amount of protein of the food which was converted into tissue proteins for new growth. The results indicated that the protein mixture contained in each of these grains can be utilized to about the same extent. The nitrogen of the proteins retained amounted to between 20 and 26 per cent of the amount ingested in all cases. The per cent of protein in the food did not appear to influence the extent of utilization.

It is now certain that the diet used in these experiments was faulty, in respect to the unsuitability of the mineral content of these grains for the maintenance of prolonged normal development. The grains are deficient in fat-soluble A, and are almost entirely lacking in the anti-scorbutic factor water-soluble C. The pig is susceptible to scurvy, and the lack of the latter was

perhaps a factor of importance in determining the outcome of the experiments. The two first named essentials certainly influenced the result of these studies, for the rate of nitrogen retention fell off toward the end of the period of observation.

96. A Method Which Affords a Fairly Accurate Comparison of the Values of Proteins.—The type of experiment which has thrown most light on the comparative values of the proteins of different foods is that first employed by McCollum and Davis (57) for showing the nature of the dietary deficiencies of the cereal grains. Their method has since been applied to other important seeds and to leaves, tubers and roots, as well as foods of animal origin (58). The details of this method have already been described (p. 27) as an illustration of the method for the biological analysis of a food-stuff. It consisted in feeding to one group of animals a natural food as the sole source of nutriment, and to other groups of animals the same food supplemented with single or multiple additions of purified food-stuffs. The interpretation of the results was based on the number of food factors which had to be improved before growth could take place, and the number which, when improved in quality, could be shown to make the diet of better quality, as revealed by fertility, success in rearing young, span of life, and general well-being.

The results showed that the quality of the proteins of the seeds of wheat, maize, oats, rice, pea, bean, flax, millet, and kaffir corn is such that, when fed at the planes of intake that can be secured by including in the diet as much of the seed as possible, the optimum condition of nutrition is not attained, even though all other factors in the diet are so adjusted as to be fairly satisfactory (59). When the latter conditions are fulfilled, the nutrition of the animals could in all cases be improved by the inclusion in the diet of a pure protein such as casein.

97. Every Seed Studied Contains Every Amino-Acid Necessary for the Nutrition of an Animal.—These studies leave no room for doubt that all the amino-acids necessary for the nutrition of an animal are contained in the proteins found in each of these foods. Certain of these are, however, present in such limited amounts as to restrict the extent to which the remaining ones, which are more abundant, can be utilized. It is for this reason that these proteins are of relatively low biological value unless supplemented by proteins from other sources, the constitution of which is such as to make good their deficiencies. The proteins of the cereal grains are of lower value than are those of

milk and eggs, or than those of certain mixtures obtained by combining two or more of these seeds.

In this chapter an attempt has been made to make clear the types of experiments which have been employed for the study of the differences in the nutritive values of proteins from different sources, and to determine the exact nature of the limiting deficiencies of each. The experimental work on which this discussion is based constitutes the most confusing phase of the literature relating to nutrition, for the reason that, although the specific problems which have been investigated have in great measure been cleared up, the original papers have, in a number of cases, failed to clearly indicate how the data later recorded modified or rendered obsolete earlier observations made by the investigators themselves. Frequent references, by persons who have made no thorough study of the literature to supposedly proven facts which were later disproved by other experiments, have convinced the author that an interpretation was here especially desirable. This is very difficult to make in an entirely clear manner without exceeding the space which could be allotted to it.

98. **The Nutritive Value of a Protein Depends on Its Yields of the Indispensable Amino-Acids.**—The work reviewed clearly establishes that the nutritive value of proteins is determined by their yields of the eighteen or more amino-acids which are formed on digestion. The more nearly these proportions correspond to the content of amino-acids in the tissues of the growing animal, the more effectively can food proteins be transformed into body proteins. There are surprising differences in the biological values of the proteins in certain of our more important foods. These will be discussed more fully later.

There is no convincing evidence that the processes of maintenance, or the repair of tissue waste, are of a lower order than those of growth, and that the needs of the former are met by a list of amino-acids which would be lacking in certain ones which are essential for the latter. Neither has it been possible to demonstrate that through the agency of the mammary gland, amino-acids (e. g., lysin) can be synthesized, for the nutrition of the young for the preservation of the species, whereas this cannot be effected for the preservation of the individual. The evidence all points to the conclusion that the transformation of food protein into milk protein is governed by the same laws as apply to growth.

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CHAPTER V

PECULIARITIES OF COMPOSITION OF PROTEINS FROM VARIOUS SOURCES

99. **Certain Amino-Acids Are Demonstrated to Be Indispensable for Animal Nutrition.**—In Chapter IV a brief account was given of the experimental studies which established the fact that the nutritive value of a protein depends upon the number and amounts of the amino-acids it yields on artificial hydrolysis or on digestion. It was shown that a protein such as gelatin, which is lacking in the amino-acids, tyrosin, cystin and tryptophan, or that a protein such as zein of maize kernel, which is lacking in lysin, is incomplete for all physiological purposes since is cannot supply all the "building stones" necessary for the construction of body proteins. No matter how much of such a protein is present in a diet, which may be entirely adequate with respect to all other food factors, nutritive disaster will speedily overtake the animal confined to it. The nutritive value of a protein or mixture of proteins depends upon the presence in its molecules of all the essential amino-acids, and upon the extent to which their proportions correspond to those existing in the body proteins they are to be transformed into. It is obvious, therefore, that mixtures of proteins unlike in their constitution may yield amounts of the several amino-acids which will tend to make them more efficient than either or any individual protein in the mixture. One protein may supplement the deficiency of the other. On these facts was based a criticism of certain of the experimental work designed to yield data showing in a quantitative way, the comparative values of different purified proteins. These purified proteins were not fed as the sole source of nitrogen (amino-acids) but were supplemented with fairly liberal additions of amino-acids in the "protein-free milk" or yeast which was included in the diet.

In order to illustrate further the differences in the constitution of individual proteins from different sources a few tables are presented which contain in summarized form the best analytical data which it has been possible to obtain by chemical methods.

Table I shows the composition of a series of animal and vegetable proteins and the sources of origin. On the left side is shown the percentage composition of each in carbon, hydrogen, nitrogen, sulphur and oxygen, which are the only elements entering into the formation of the simple proteins. These elements are designated by the symbols, C, H, N, S and O respectively. On the right-hand side in their respective columns are tabulated the number of atoms of each of these elements which a single molecule of the protein is believed to contain, and in the column headed "Molecular Weight" are the numbers which indicate approximately the weight of a single protein molecule as compared with an atom of hydrogen which is taken as unity.

100. **Elementary Composition of all Proteins Is of the Same Order.**—The most interesting information to be gained from this table, is the remarkable similarity of the proteins from various sources in respect to their content of carbon, hydrogen and oxygen, and their relatively wide differences in nitrogen and sulphur content. Ovalbumin of the hen's egg contains but 15.51 per cent of nitrogen, whereas amandin from the almond contains 19.32 per cent. Legumin from the bean contains but 0.385 per cent of sulphur, while serumalbumin from human blood contains 2.25 per cent of this element, or nearly six times as much for equal weights of the two substances.

101. **The Hausmann Method of Analysis of Proteins and the Data Obtained.**—In Table I is shown data regarding the constitution of different proteins as revealed by another method of analysis known as the Hausmann method. There is in every protein a complex which, when boiled for a few hours with moderately strong mineral acids, yields ammonia. In the table the per cent of the total nitrogen of the protein which is convertible into ammonia is tabulated in the first column under NH_3-N. There are three diamino-acids derived from proteins, which are sharply differentiated from all the others by their basic character, that is, they have an alkaline reaction when in solution. They can be precipitated together by means of phosphotungstic acid, and thus separated sharply from all the other constituents of the protein molecule. The remaining amino-acids formed on hydrolysis or digestion of proteins are collectively designated as mono-amino acids. The yields of these are tabulated in the third column. When proteins are heated with acids as is necessary in the method of analysis under discussion, there is always formed a certain amount of black, insoluble

TABLE I

Elementary Composition and Molecular Weights of Proteins.*

Percentage compositions	C	H	N	S	O	Formula	C	H	N	S	O	Molecular weight
						Plant Proteins						
1. Almond	51.30	6.90	19.32	0.429	22.05	1. Amandin	638	1030	206	2	206	14930
2. Pea	52.64	6.95	17.25	0.426	22.73	2. Vignin	660	1010	185	2	214	15038
3. Bean	51.72	6.95	18.04	0.385	22.90	3. Legumin	718	1158	214	2	238	16642
4. Maize	55.23	7.26	16.13	0.600	20.78	4. Zein	736	1161	184	3	208	15993
5. Soy bean	52.12	6.93	17.53	0.710	22.71	5. Glycinin	780	1248	206	4	255	17700
6. Barley	54.29	6.80	17.21	0.847	20.53	6. Hordein	675	1014	181	4	194	14880
7. Hempseed	51.50	7.02	18.69	0.88	21.91	7. Edestin	624	1021	193	4	199	14523
8. Bynin	55.03	6.67	16.26	0.84	21.20	8. Bynin	706	1026	180	4	204	15410
9. Wheat	52.72	6.86	17.66	1.027	21.73	9. Gliadin	685	1068	196	5	211	15568
10. Para nut	52.18	6.92	18.30	1.086	21.51	10. Excelsin	642	1018	192	5	198	14738
11. Wheat	53.02	6.84	16.80	1.280	22.06	11. Leukosin	663	1026	180	6	207	15006
						Animal Proteins						
12. Ox	54.98	7.20	16.89	0.42	20.51	12. Globin	700	1098	184	2	196	15274
13. Ox	52.68	6.83	16.91	1.10	22.48	13. Fibrin	645	1004	178	5	207	14708
14. Horse	52.71	7.01	15.85	1.11	23.32	14. Serumglobulin	628	1002	160	5	209	14310
15. Horse	52.93	6.90	16.66	1.25	22.26	15. Fibrinogen	679	1062	183	6	207	15276
16. Muscle	52.82	7.11	16.67	1.27	22.03	16. Myosin	660	1074	181	6	208	15048
17. Egg	52.75	7.10	15.51	1.616	23.02	17. Ovalbumin	696	1125	175	8	220	15703
18. Cow's milk	52.19	7.18	15.77	1.73	23.13	18. Lactalbumin	644	1064	166	8	214	14792
19. Horse	52.99	7.01	15.93	1.93	22.14	19. Serumalbumin	662	1051	171	9	207	14989
20. Man	52.25	6.65	15.88	2.25	22.95	20. Serumalbumin	684	1045	178	11	225	15697
21. Horse	54.64	7.09	17.38	0.39	20.16	21. Oxyhaemoglobin	758	1181	207	2	210	16655
22. Man	54.57	7.11	16.38	0.568	21.04	22. Oxyhaemoglobin	758	1185	195	3	219	16667
23. Cow's milk	53.13	7.06	15.78	0.800	22.37	23. Casein	708	1130	180	4	224	15982
24. Egg yolk	51.56	7.12	16.23	1.028	23.24	24. Ovovitellin	671	1112	182	5	227	15628

* Osborne, T. B. Zeit. f. analyt. Chem., xli, 25, 1902.

nitrogenous substance called humin. It has been shown that most of this comes from the decomposition of a single compound called tryptophan, one of the mono-amino acids. Some proteins are entirely lacking in tryptophan. An example of such a protein is zein of the maize kernel. In the column headed "Total N," is given the per cent of nitrogen in the samples of the proteins employed in the analyses.

An inspection of this table shows that the amount of nitrogen in the protein molecule which is convertible into ammonia under the conditions of the analysis, varies from as low as 6.46 per cent in legumelin of the pea or bean to as high as 23.78 per cent in gliadin of wheat. In contrast with the proteins of animal origin, it will be noticed that many of the proteins of vegetable origin contain two or three times and a few more than four times the amount of nitrogen in this special ammonia-yielding complex. This is one of the types of data which, as early as 1905, clearly showed that the proteins differ to a great extent in their constitution, and that food proteins are in most cases quite unlike the proteins which compose the muscles and organs of the body.

The method of analysis by means of which the data in Table II were secured, is not a very searching one, and fails to yield as detailed information as is desired for physiological reasoning. For this purpose the differences in the yields of the diamino-acids (bases) in different proteins do not, except in a few instances, contrast markedly with each other. In the case of glutenin, gliadin, hordein and zein, the principal proteins of the wheat, barley, and maize kernels, the content of the basic amino-acids falls far below that present in any of the animal proteins. As will be seen from the next table to be considered, there is more to be learned about this fraction of the protein molecule than the above data reveal. There are three substances in this group, the names of which are arginin, histidin and lysin. Different proteins show marked variation in the content of one or another of them.

102. **The Content of Arginin, Histidin and Lysin in Individual Proteins.**—Table III (p. 96) contains analytical data obtained by a refined method for the estimation in proteins of the three diamino-acids, arginin, histidin and lysin. This method was devised by Kossel. In skilful hands it yields very accurate results. It will be noted that the histidin content of plant proteins varies much less than does that of either arginin or lysin. Yet the extreme values for this constituent of the protein molecule

TABLE II

DISTRIBUTION OF NITROGEN IN PROTEINS*

TOTAL N = 100

	NH_3 N	*Basic Amino Acids* N	*Mono-Amino Acids* N	*Humin* N	*Total* N
Vegetable Proteins:					
Conalbumin (egg white)	7.51	25.82	65.11	1.61	16.11
Phaseolin (bean)	10.74	24.50	62.85	1.79	16.20
Glycinin (pea)	12.09	22.63	64.58	.68	17.45
Legumelin (pea, bean) ..	6.46	23.06	68.12	2.36	16.09
Leucosin (wheat)	6.85	20.67	69.87	2.54	16.93
Glutenin (wheat)	18.86	11.72	68.32	1.09	17.49
Gliadin (rye)	23.78	5.49	70.27	.79	17.66
Hordein (barley)	23.30	4.47	69.96	1.33	17.21
Zein (maize)	18.41	3.03	77.56	.99	16.13
Globulin (wheat)	7.72	37.14	53.39	1.52	18.39
Globulin (coca nut)	7.35	32.79	59.09	.75	18.48
Globulin (squash seed) ..	6.91	32.25	59.64	1.18	18.51
Globulin (cotton seed) ..	10.30	30.63	59.06	....	18.64
Edestin (hemp seed)	10.08	31.70	57.83	.64	18.64
Excelsin (para nut)	8.87	31.47	59.94	.92	19.30
Corylin (hazel nut)	11.57	30.26	56.31	.89	19.00
Amandin (almond)	16.04	21.84	60.08	.89	19.00
Globulin (castor bean) ..	10.45	30.08	58.66	.64	18.75
Corylin (walnut)	9.44	28.71	61.09	.79	18.84
Conglutin (a) (lupine) ..	11.84	29.05	58.00	1.00	17.90
Conglutin (b) (lupine) ..	14.55	28.17	56.56	.76	18.21
Legumin (pea)	9.40	28.82	60.27	.94	17.97
Globulin (flaxseed)	10.82	25.81	62.06	1.18	18.48
Vicilin (pea, bean)	10.40	27.76	60.60	1.22	17.11
Vignin (pea)	11.07	25.39	62.66	1.45	17.25
Globulin (sunflower seed)	13.83	22.98	62.00	1.29	18.58
Stizolobin (Velvet bean)	10.51	27.96	60.06	1.36	16.40
Arachin (Peanut)	11.10	27.13	60.50	1.20	18.28
Animal Proteins:					
Vitellin (egg yolk)	7.67	28.56	62.41	1.35	16.28
Casein (cow's milk)	10.30	22.84	66.00	1.34	15.62
Ovalbumin (egg)	8.64	21.27	68.21	1.87	15.51
Chicken muscle	7.45	29.98	59.85	2.43	16.09
Halibut muscle	6.70	30.18	60.73	2.37	16.40
Scallop muscle	6.33	26.51	64.81	2.34	17.05
Beef muscle	5.50	27.32	64.52	2.65	16.18

*Compiled from the papers of T. B. Osborne and of C. O. Johns.

TABLE III

CONTENT OF ARGININ, HISTIDIN AND LYSIN IN PROTEINS.*

	Histidin	*Arginin*	*Lysin*
Vegetable Proteins:			
Globulin (Buckwheat)	0.88	23.67	8.61
Globulin (Squash seed)	2.42	14.44	1.99
Excelsin (Para nut)	2.50	14.29	1.64
Edestin (Hemp seed)	2.19	14.17	1.65
Globulin (Cotton seed)	3.46	13.51	2.06
Stizolobin (Velvet bean)	3.81	14.13	10.02
Globulin (Castor bean)	2.74	13.19	1.54
Amandin (Almond)	1.87	12.16	0.72
Legumin (Pea)	1.69	11.73	4.98
Legumin (Vetch)	2.94	11.06	3.70
Conglutin A (Lupine)	2.51	10.93	2.73
Vicilin (Pea)	2.17	8.91	5.40
Glycinin (Soy bean)	2.10	7.69	3.39
Vignin (Cow pea)	3.08	7.20	4.31
Glutelin (Maize)	3.00	7.06	2.93
Leucosin (Wheat)	2.83	5.94	2.75
Legumelin (Pea)	2.27	5.45	3.03
Legumelin (Soy bean)	2.04	5.35	4.91
Phaseolin (Kidney bean)	2.62	4.87	4.58
Glutenin (Wheat)	1.76	4.72	1.92
Gliadin (Wheat)	0.58	3.16	1.33
Gliadin (Rye)	0.39	2.22	...
Hordein (Barley)	1.28	2.16	...
Zein (Maize)	0.82	1.35	0.00
Animal Proteins:			
Ovovitellin (Egg yolk)	1.90	7.46	4.81
Beef muscle	2.66	7.47	7.59
Scallop adductor muscle	2.02	7.38	5.77
Chicken muscle	2.47	6.50	7.24
Halibut muscle	2.55	6.34	7.45
Conalbumin (Egg white)	2.17	5.07	6.43
Ovalbumin (Egg white)	1.71	4.91	3.76
Casein (Cow milk)	2.50	3.81	5.95
Lactalbumin	2.06	3.23	9.16

* This table is compiled from various sources, especially the papers of Osborne and of Johns.

range from 3.81 per cent in stizolobin, a globulin from the velvet bean, to 0.39 per cent in gliadin from rye. The content of arginin in different proteins varies in a surprising degree. Thus a globulin of buckwheat yields 23 per cent arginin, whereas zein of the maize kernel contains but 1.35 per cent. Among the vegetable proteins the yield of lysin is generally very low in com-

parison to that obtained from the proteins of animal tissues. The extreme limits of the yield of lysin in plant proteins range from 10.2 per cent in the globulin of the velvet bean to complete absence in zein of maize.

A comparison of the relative amounts of these three digestion products in proteins of vegetable with those of animal origin reveals at once a remarkable fact. While the amount of histidin is of the same order in the two classes, arginin is found in many proteins of seeds in quantities greatly in excess of any of the proteins of animal tissues. The only vegetable proteins yet studied which exceed, in their content of lysin, the muscle proteins of animals, are those of the velvet bean and buckwheat (1).

TABLE IV

PER CENT OF GLUTAMIC ACID YIELDED BY PROTEINS.*

Vegetable Proteins:	
Gliadin (Wheat)	42.98 per cent.
Gliadin (Rye)	37.80
Hordein (Barley)	43.19
Zein (Maize)	26.17
Leucosin (Wheat)	5.72
Glutenin (Wheat)	23.40
Amandin (Almond)	23.14
Edestin (Hemp seed)	14.00
Corylin (Hazel nut)	17.94
Phaseolin (Bean)	12.33
Vignin (Pea, bean)	16.30
Legumin (Vetch)	16.48
Glycinin (Soy bean)	19.46
Conglutin (Yellow lupine)	30.05
Animal Proteins:	
Casein (Cow milk)	10.77
Ovalbumin (Egg)	9.01
Conalbumin (Egg)	7.00
Vitellin (Egg yolk)	12.95
Serum albumin (Horse)	7.70
Serum globulin (Horse)	8.50
Halibut muscle	10.13
Chicken muscle	16.48
Scallop muscle	14.88
Dog tissues, entire body	14.00
Rabbit tissues, entire body	14.14
Hen tissues, entire body	12.02

*Compiled data from various sources, especially the papers of T. B. Osborne and E. Abderhalden.

It was the marked deficiency of most of the vegetable proteins in lysin in contrast to the animal proteins that led Osborne and Mendel and others to believe at one time that this amino-acid was frequently the limiting factor which determined the nutritive value of food proteins. The investigations relating to this phase of nutrition have been described in the preceding chapter.

103. **Variation in the Glutamic Acid Content of Proteins.** —Table IV shows the composition of a number of proteins of animal and vegetable origin with respect to glutamic acid. This amino-acid is a never-failing component of all vegetable proteins and of all animal proteins except the protamins, which have been found in the spermatozoa of fish. It will be seen that this hydrolytic product is frequently much more abundant in vegetable proteins than in animal tissues or in egg or milk proteins.

With these data available, it is easy to understand why food proteins show great variations in nutritive value, for this depends upon the efficiency with which they can be transformed during growth, or in the course of the repair of tissue waste into tissue proteins. They also reveal the logic of taking a mixture of proteins in the food, since by this means there is a probability that the deficiencies of one protein may be in some measure corrected by another which may yield liberal amounts of those amino-acids it lacks wholly or in part. Since in practice both in human nutrition and animal nutrition several proteins are always taken together, either when vegetable or animal tissues are used as food or when the by-products of manufacture are employed as supplements to naturally occurring foods, it is of great economic importance to discover what foods contain proteins which possess high supplementary values. Protein is the most expensive component of foods or feeding-stuffs, and agricultural economics can be greatly advanced by scientific discovery in this field. In human nutrition the element of economy, in ordinary times, enters less as a factor than physiological well-being, but it would appear that it is no less important here that a protein supply of high biological value be provided in the diet. It seems logical to prefer to serve the needs of the body by providing it with the optimal amount of such proteins as can be utilized very effectively rather than to require it to digest and assimilate an excessive amount of proteins of low value. In this connection it must be remembered that the moiety of amino-acids which cannot be properly matched with each other so as to form the necessary structures have to be promptly destroyed and their

degradation products eliminated as waste. This would impose an unnecessary burden on the organs concerned with the metabolism of the nitrogenous components of food.

104. **Conditions Necessary for the Comparison of Proteins by Feeding Experiments.**—In order to study the effectiveness with which the proteins of one food supplement those of another it is essential that diets be planned so as to be highly satisfactory with respect to all other factors besides protein. The natures of the deficiencies of all the foods studied must first be well understood, so that any mixtures employed in experiments designed to reveal the biological values of combinations of proteins may be supplemented with respect to inorganic salts, the essential vitamins, etc. Under such considerations the success or failure of growth, reproduction or other function in the animals will turn solely on the quality of the proteins of the experimental diet. In Chapter VI the dietary properties of many of the more important of our foods are given in detail, so that it is now possible to appreciate the method employed in the study of the protein values of combinations of these articles of diet.

105. **Methods of Procedure for Comparing the Biological Values of Individual Proteins.**—Several lines of procedure offer prospects of successful comparison of the relative biological values of mixtures of proteins. One is to feed a series of groups of young and growing animals a diet similarly constituted and deriving its protein from the same source, but with the per cent of protein adjusted in the series from very low to very high levels. From the rate of growth of the animals an idea can be gained as to the least amount of protein from the sources studied, which just suffices to maintain animals without growth and to induce growth at subnormal rates, or at the maximum rate.

Another method of investigation is to utilize female animals nursing litters of young. By adopting a standard size for the litters, and by observing the success with which the mothers induce growth in their young when the diet contains different percentages of protein but is otherwise of uniform composition, an approximately quantitative comparison of the values of the proteins from different sources can be made.

Osborne and Mendel (2) made attempts, in their studies with isolated proteins, to determine their relative values by observing the growth of animals which ate the same amount of food in the same number of days and gained the same amount in weight. The protein factor was the only variable. It is very difficult to

conduct experiments in this manner, and Osborne and Mendel (3) attempted to develop another method by restricting the protein so that it became the factor which determined the rate of growth, and then attempted to discover the concentration of protein in the diet promoting the greatest gain of body weight relative to the protein ingested. To accomplish this result they supplied the experimental animals with foods containing different percentages of the same protein. Using this method they secured data which is illustrated by the following table:

Protein.	*Initial Body Weight. Grams.*	*Protein in Food. Per Cent.*	*Intake Per Gram of Gain.*		*Gain Per Gram of Food.*	*Gain Per Gram of Protein. Grams.*
			Food. Grams.	*Protein. Grams.*		
Lactalbumin ..	62	16.2	3.3	0.52	0.31	1.93
	61	"	2.6	0.42	0.39	2.41
	73	"	3.4	0.54	0.30	1.86
	67	"	3.8	0.60	0.27	1.67
Average			3.3	0.52	0.32	1.97
Lactalbumin ..	71	10.3	3.6	0.37	0.28	2.74
	63	"	4.0	0.42	0.25	2.41
Average			3.8	0.40	0.27	2.58
Lactalbumin ..	64	7.9	4.0	0.31	0.25	3.18
	70	"	4.5	0.35	0.22	2.83
Average			4.3	0.33	0.24	3.01
Lactalbumin ..	66	6.2	6.3	0.39	0.16	2.58
	67	"	6.0	0.37	0.17	2.69
Average			6.2	0.38	0.17	2.64
Lactalbumin ..	63	4.9	8.6	0.42	0.12	2.40
	63	"	8.9	0.43	0.11	2.32
Average			8.8	0.43	0.12	2.36
Lactalbumin ..	68	3.3	18.7	0.62	0.05	1.63
	67	"	24.6	0.82	0.04	1.23
Average			21.7	0.72	0.05	1.43

In a similar study in which casein was the protein used, the protein intake was in most cases higher than in the lactalbumin

experiments. For the sake of comparison the results are given below in condensed form.

Protein .... Casein
Per cent in food 17.4
Weights of experimental animals .... 58-76 grams
Intake per gram of gain { Food....3.1; 4.0; 3.0; 3.5; 3.9; 3.1; 3.5; 3.0; 3.4. Average, 3.4.
Protein..0.54; 0.70; 0.53; 0.61; 0.68; 0.53; 0.61; 0.52; 0.59. Average, 0.59.

Protein .... Casein
Per cent in food 14.7
Weights of experimental animals .... 64-67 grams
Intake per gram of gain { Food....4.1; 3.5; 3.0. Average, 3.5.
Protein..0.60; 0.51; 0.44. Average, 0.52.

Protein .... Casein
Per cent in food 12.0
Weights of experimental animals .... 63-69 grams
Intake per gram of gain { Food....4.2; 3.5; 3.5. Average, 3.7.
Protein..0.50; 0.42; 0.42. Average, 0.45.

Protein .... Casein
Per cent in food 9.3
Weights of experimental animals .... 64-65 grams
Intake per gram of gain { Food....8.9; 6.4; 7.4. Average, 7.6.
Protein..0.83; 0.59; 0.68. Average, 0.70.

106. **Individual Variation in Rate of Growth of Rats.**—From the data given it will be seen that under the same experimental conditions and on the same diet the variation in gain of body weight amounted to as much as 75 per cent and the gains per gram of protein ingested varied as much as 10 to 30 per cent in different animals. The most plausible explanation of the lack of uniformity in the rate of growth in their animals was that their stock included animals of very low vigor as well as those of greater vitality. There was thus introduced into their interpretation an averaging of growth in animals not able to make efficient use of food for growth with growth in others in which growth impetus and synthetic powers were greater. *If we desire to learn the extent to which a food protein during growth can be converted into body proteins it would be more logical to accept only the greatest gain observed in any animal, discarding all other results, rather than to average the gains made by good and poor ones.* From their data Osborne and Mendel estimate that the gain of weight per gram of protein eaten during a period of eight weeks was for lactalbumin 2.34 and for

casein 1.70 grams. In three experiments with casein fed at 12.0 per cent of the food mixture, the animals made an average gain of 2.25 grams per gram of casein consumed. One animal attained a gain of 2.39 grams and another of 1.99 grams. Their results are not very convincing as proof of the superiority of this method as a measure of the relative biological value of proteins. In interpreting the value of the data in the tables in which lactalbumin and casein are compared, it should be borne in mind that neither protein was fed as the sole source of nitrogen, but that it was supplemented with the nitrogen of 28.2 parts of protein-free milk. It has already been pointed out that lactalbumin is actually an incomplete protein and is incapable of inducing any growth whatever unless its deficiencies are made good by some other source of amino-acids. The extent to which the protein-free milk nitrogen supplemented the proteins in these experiments was very great. Thus in the diets where 16 per cent of lactalbumin was included, 8.3 per cent of the total nitrogen of the diet came from protein-free milk. In the diets which contained 10.0 per cent, 6.2 per cent and 3.3 per cent of lactalbumin, the per cent of the total nitrogen derived from protein-free milk was 13.4 per cent, 22.4 per cent and 41.0 per cent, respectively. The recorded data of Osborne and Mendel do not in any sense represent a comparison of the biological values of casein and lactalbumin, and actually give a wholly false impression. It has already been pointed out that they were forced to revise because of the faulty technique in their experiments their views concerning the values of several of the proteins which they studied most extensively (4).

107. **Conditions Under Which Energy and Protein Are Used Most Economically by Growing Animals.**—The data of Osborne and Mendel discussed above, have an interest quite apart from their worth as quantitative comparisons of the relative values of proteins. They support the view that "Economy of food can be effected only by supplying the young animal with as much as it will eat; economy of protein only by reducing the nutritive ratio below that at which the normal rate of growth can be maintained." This principle appears to be established, but it is quite another matter to determine whether or not economy of protein utilization obtained by the means just mentioned, makes for physiological well-being. The studies of McCollum and Simmonds, to be described later, point to the desirability, from the standpoint of the long maintenance of vigor,

of a liberal supply of protein in a diet which is otherwise satisfactorily constituted with respect to all other factors.

108. **The Method of McCollum, Simmonds and Parsons for Comparing the Nutritive Values of Proteins.**—A procedure introduced by McCollum, Simmonds and Parsons (5) for the study of the relative values of different proteins, or for the supplementary values of proteins from different sources, involves feeding a series of groups of animals on a series of diets which are of uniformly excellent quality with respect to all factors except quality of protein. The diets are all made to contain 9 per cent. of total protein, which may be derived from a single food or from two or more sources as stated above. On such diets young rats are observed during the entire growth period and thereafter up to the time when pronounced development of senile characters are noted. The groups contain animals of both sexes, and the fertility and infant mortality are carefully observed. The behavior of the animals, especially with respect to a tendency to destroy their new-born young when the protein supply is unsatisfactory, is also carefully recorded.

This method was the outgrowth of considerable experience in searching for the most satisfactory procedure for making a comparison of the effectiveness of different foods as protein supplements for one another. McCollum and his co-workers had conducted numerous experiments in feeding animals diets containing different percentages of protein, and otherwise enhanced so as to make them of good quality, and had made an effort to study the relative values of purified proteins and of the mixtures of proteins contained in individual natural foods, both for growth and for the replacement of the nitrogen lost through endogenous or tissue metabolism (6). In the early studies too little was known about supplementing factors other than protein. None of these results are to be regarded as very satisfactory for the reason that factors other than protein in the experimental diets employed, were not always satisfactorily improved to make the results turn entirely upon the quality of the proteins of the food.

109. **Importance of Quantitative Records of Food Consumption.**—Many of these studies were severely criticized by Osborne and Mendel because, when rats were employed as experimental animals no accurate records were kept to show the exact amounts of food consumed by each individual. They pointed to the great differences in amount of food eaten by different rats as evidence that there must, in this kind of work,

be a correlation between food consumption and growth. Osborne and Mendel were able by using large amounts of fat to convert their foods into a paste, which could be placed in a glass tube provided with a rod acting as a plunger. Each rat was kept in an individual cage. Food was from time to time expelled from this device into the feeding dish. Employing this device in all their experiments they were able to furnish figures for food consumption.

McCollum was not able to secure a quantitative record of food intake in his animals (rats) until about 1915, for he and his co-workers employed diets in the form of finely ground powders. These consisted of either purified food substances, or of natural foods with certain additions of salts, fats, etc.

110. **A Feeding Device for Measuring the Food Consumption of the Rat Fed Dry Powdered Food.**—Their plan did not admit of the inclusion of large amounts of fat in their food mixtures, because this procedure diluted so much the mineral content, protein content, etc., of any natural food under investigation, that it made it impossible to feed sufficient amounts of grains, legume seeds, etc., to give an accurate picture of their dietary properties. It was imperative, for their purposes that rats should be fed with dry powders. A device was finally designed which left little to be desired for the quantitative feeding of such powders. This consists of a tin pie plate suspended from the roof of the cage by means of three wires which are attached to the rim of the pan so that they occupy the position at the angles of an equilateral triangle. These wires are brought together like the tepee lodgepoles, being connected with a ring by means of a small link for each wire. A wire is passed through perforations in the rim of the pan so as to cross it at a line, the center of which lies half the diameter of a pint tin cup from the center of the pie pan. This wire is bent so as to form a circle which circumscribes the center of the pan. The circle is just large enough to admit of the insertion of a pint tin cup without a handle. The feeding cup is thus held securely in the center of the pan. Inserted in the mouth of the tin cup is a cover so made as to fit firmly into the cup like the lid of a dinner pail. The top of this cover is shaped much like the top of a cuspidor, being funnel-shaped and having a hole in the center, through which the rats can secure the powdered food. In order to minimize the chances of scattering food, the cover is made about double the diameter of the tin cup, so that it forms a large funnel which tends to return the traces of

powdered food to the cup should any be removed and not eaten by the rat. If this device is not filled more than half full, it is impossible for a rat to scratch any of the food from the cup. It must eat through the hole in the center. The size of this hole may be gauged, if desired, to the size of the rats used in experiment.

With this device McCollum and Simmonds found it easy to secure records of food intake which certainly are accurate to within 1 per cent. Since they did not keep their animals in individual cages, but in groups of four to eight or ten in one large cage, most of their records showed the food consumption of the group and not of any one individual. This practice was followed because of the great increase which it made possible in the number of animals which could be kept under observation, thus making feasible the conduct of a much larger number of experiments.

Experiments with feeding various sources of proteins at different percentages of the food mixtures brought to light the fact that there are few sources of proteins among our ordinary foods sufficiently high in quality that a diet containing but 9 per cent of protein, and otherwise satisfactory will be adequate for the promotion of growth at the maximum rate and to the full adult size, and for the maintenance to an advanced age of a high health standard in the rats confined to it. Only such proteins will, when fed at this plane of intake, serve to maintain the vitality of rats at a point where their fertility will be high, and the nursing of their litters satisfactory.

III. **Method of Expressing the Relative Nutritive Values of Proteins.**—Results characteristic of excellent nutrition can be secured with diets planned as just described, in which the proteins are derived solely from milk, kidney, or a mixture of certain seeds, notably of rye and flaxseed oil meal. So far as experience has progressed, however, such effects cannot come from restricting rats to any diet containing less than 9 per cent of protein from any source. McCollum, Simmonds and Parsons (7) felt justified in classing as excellent, any protein or protein mixture which would support nearly optimal nutrition over periods approximating two-thirds or more of the normal span of life of the rat, when fed in amount corresponding to 9 per cent of the food mixture. Instead of trying as Osborne and Mendel had done, to establish absolute values for the proteins, they undertook only to compare any protein or mixture of proteins with

some protein which, according to the definition just given, would be classed as excellent, or in other words, about as good as any proteins known from the nutritive standpoint.

In order to do this, McCollum, Simmonds and Parsons simply confined groups of four to six rats in a cage 24 x 24 x 20 inches in dimensions, screened on all sides, or on three sides with wire cloth of one-quarter inch mesh. The food records always showed the amount consumed in the group. Note was kept of the number of times, with dates, when the standard quantity of one kilogram of food was prepared. The animals were not able to dispose of their food otherwise than through eating. It was believed that a more detailed record of individual food consumption would add little if any value to the results or make their interpretation more significant. Since Osborne and Mendel have repeatedly emphasized their belief that feeding studies of this nature fail of their purpose unless accurate food consumption records are kept, it is incumbent upon McCollum and his co-workers to defend their system against this criticism.

112. **Changing Food Consumption with Growth.**—When a young animal is growing there is a constantly increasing need for food, and a progressive increase in consumption is observed. If two animals are fed diets which are alike except for their protein content, or in the nature of their proteins, one may grow because the protein of its food is well constituted, while the other may fail because the protein in its food is deficient in some respect. Comparison of food intake and consequently of protein consumption is not practicable in these animals since the difference in size is becoming constantly more pronounced. Osborne and Mendel have made an elaborate study of food consumption in rats under different dietary restrictions, and their data are of great interest in connection with the present question (8).

They found that rats growing well on a diet containing 9 per cent of casein when a small amount of cystin was added, frequently ate no more food in terms of calories, and ingested no more protein than did rats which were growing no better on even larger percentages of casein without the addition of cystin. They concluded in this instance: "It thus appears that a marked deficiency in any essential ingredient of the diet does not lead to a corresponding compensatory increase in food intake."

113. **Appetite as a Factor Governing Food Consumption.**—Their study of the rôle of appetite in regulating food consump-

tion has led them to state: "The experience which we have gained in measuring the food eaten by many rats at all periods of their growth has given us the conviction that the intake of the individual is determined in large measure by the energy requirement at any given period" (8) (p. 358). To quote from page 359 of the same paper, "At any rate the animals do not consume *proportionately* more of the artificial ration because it happens to be decidedly poor in protein; but roughly speaking, they appear to limit their feeding to the amount of food yielding approximately the requisite energy." This view is in accord with that of Rubner (9), who found that food which a dog will eagerly devour when in a room at the temperature of 0° C., he will in part refuse when the temperature is raised to 33°, under which conditions, his energy requirements are much lower.

In a later publication Osborne and Mendel (10) showed the food consumption of rats fed diets containing varied amounts of fat. Since fat has about double the energy value of protein or carbohydrate, much smaller amounts of the fat-rich diets would furnish the required amount of energy needed than would be necessary with the fat-poor diets. In all cases food consumption was found to be regulated by energy needs and was comparable in animals on diets of similar calorific value.

It is only necessary to point out that McCollum and his co-workers have throughout their studies employed diets low in fats, and very much alike in their energy values. Food intake should have been, therefore, according to Osborne and Mendel's experience, entirely comparable. Numerous records obtained in recent years in the laboratory at Johns Hopkins University have shown clearly that this is the case. Quoting again from the paper of Osborne and Mendel from which extracts have already been presented (p. 523), "McCollum does not state the amount of food which his experimental rats ate; but if we assume that they ate quantities of the type of food which he employed in amounts approximately equal to those eaten by rats in our experiments on foods of corresponding calorific value, the difference between the results of his experiments and ours disappear." The force of their repeated criticisms of the work of McCollum and his co-workers largely vanish with the recording of this comment.

Owing to faults in the technic employed in earlier experiments, we find ourselves to-day with extremely little information concerning the manner and extent to which any purified proteins

supplement one another, and to the manner and extent to which they are by combination mutually enhanced in biological value. On the other hand we have a very considerable amount of accurate knowledge concerning the supplementary dietary relations among certain of our most important food-stuffs. To these supplementary relations we will now turn our attention.

114. **Supplementary Values of Proteins from Different Sources.**—Employing the method described above, in which an effort is made to determine the extent to which any protein or mixture of proteins falls short of the best quality yet observed in proteins, McCollum, Simmonds and Parsons made an elaborate study of a long list of simple combinations of two natural foods, supplemented with respect to all factors other than protein. In all cases the protein constituted 9 per cent of the diet since this plane of intake is a critical one even when the protein is of good quality. The life histories of experimental rats confined to such diets show clearly whether the protein content of any diet made on the plan described should be classed as poor, good or excellent. The details of the extent to which the animals are able to grow, perform the functions of reproduction, and retain the characteristics of youth, enable one to differentiate between shades of quality in this moiety of the diet, to a degree of refinement not equalled by any other method of study.

Employing this method, McCollum, Simmonds and Parsons studied the relative values of the proteins of kidney, liver and muscle of the ox as the sole source of protein. Of these kidney is easily shown to be superior to the other two tissues. As sources of amino-acids liver is second, and muscle third in value.

In Chart 4 are presented curves showing the extent to which young rats are able to grow when confined to diets which were comparable in all respects and the protein came from a single source. With the exception of the diet in which milk proteins were supplied as the sole source of nitrogen, the diets described in this chart derived their protein from a single seed, either a cereal grain or a legume seed.

115. **Proteins of Extraordinary Value.**—Kidney, liver and milk proteins stand out as a group of foods containing proteins of unusual value. Among the cereal grains, wheat easily stands first in the quality of its proteins. There is little reason to attempt to place rye, maize, barley, flaxseed oil meal, rolled oats and kaffir corn in their order of values as the sole source of nitrogen in the diet. All that can safely be said is that barley and rye appear to be slightly better than the other seeds named.

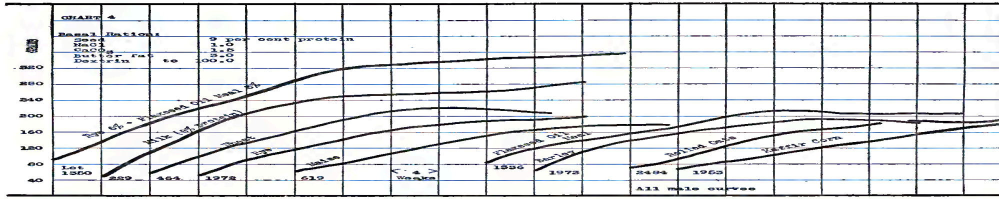

CHART 4.—In this chart are shown a series of growth curves of rats which were fed on diets which were comparable in every respect except in the quality of their proteins. All the diets contained 9 per cent of protein except Lot 229, which contained but 8 per cent. It will be seen that rye and flaxseed oil meal furnish a combination of proteins of extraordinary nutritive value, for growth was rapid and the ultimate size attained was great. When the remaining curves are compared it will be seen that 9 per cent of wheat protein produced growth a little less satisfactory than did 8 per cent of milk proteins. None of the other proteins were as good as those mentioned. The steepness of the curve denotes the excellence of the proteins.

Kidney proteins alone, when fed at 9 per cent of the food mixture, appear to give excellent nutrition, and the fact that it is not entirely adequate appears only in the falling off of the fertility of the animals to decidedly below the maximum. As is the rule with families of rats confined through several generations to a monotonous diet, which is faulty in a slight degree, each succeeding generation is smaller when its growth is completed, and in a few generations, indeed, the strain dies out.

116. **Proteins of Cereal Grains Do Not Supplement Each Other.**—Without exception it has been found that two cereal grains fail to supplement very well the protein deficiencies of one another and accordingly animals do little or no better when fed 9 per cent of protein derived from two cereals than they do when confined to one. There are, however, some remarkable instances of effective supplementing between certain cereal grains and certain of the legume seeds. Conspicuous among these successful combinations is wheat and pea. When fed with all necessary additions other than protein, a group of young rats grew to the full adult size and the females were very fertile. There was a slight decrease in size in succeeding generations, but the females of the third generation were still vigorous enough to produce and rear young. In this diet the wheat furnished two-thirds and the peas, one-third of the total proteins.

Maize kernel and pea, fed in combination parallel to the wheat and pea ration just mentioned, proved almost a failure for the nutrition of the rat. The young animals confined to this diet, the only fault of which lay in its protein moiety, failed to grow as rapidly as they should, and were permanently undersized. Fertility in the females was very low, and the second generation of this family after weaning increased very slowly in weight. See Charts 5 and 6.

It would take us too far afield to comment in detail upon the relative merits of all the numerous protein mixtures which were included in this study. Some of these are tabulated in condensed form in Tables V, VII and IX. Perhaps the most striking thing brought out by this series of experiments is the fact that in certain cases animal tissues are more effective for enhancing the value of cereal proteins than are the proteins of milk. Thus a mixture of rolled oats supplying 6 per cent and milk supplying 3 per cent of protein was found to be inferior to a similar combination of oats and liver, but about equal in value to mixtures of oat proteins and beef muscle or beef kidney, where the cereal

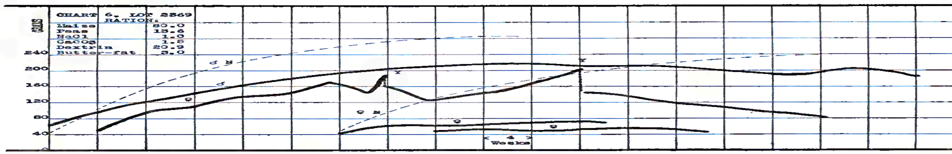

CHART 5.—This chart shows the amount of growth which it is possible to induce in a rat which is confined during growth to a diet containing but 9 per cent of protein derived from maize and peas. All the deficiencies of a mixture of maize and peas were made good by the addition of the inorganic salts and butter fat. The growth was stunted, and the fertility low. The young born of the rats which had grown on this diet were never able to grow after they were weaned, and lived only five to six months. This chart should be contrasted with Chart 6 in which the diet was essentially similar, except that the proteins were derived from a mixture of wheat and peas instead of maize and peas. The former mixture gives proteins of much greater nutritive value than does the latter combination. It is a matter of great practical importance to so combine our natural foods as to secure protein mixtures of high biological value. (See Table IX, p. 118.)

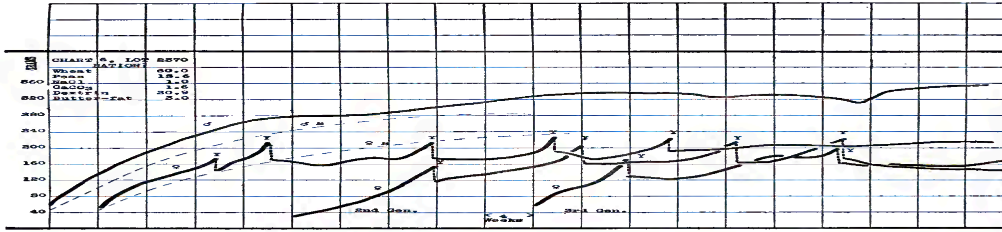

CHART 6.—The curves in this chart should be compared with those in Chart 5. The two diets were alike in their biological value except in the quality of their proteins. Lot 2370 derived its proteins from wheat and peas and were able to grow well and showed high fertility because this combination contains proteins which supplement and enhance each other. Maize and pea proteins do not, on the other hand, enhance each other's values when they are combined. In animal production as well as in human nutrition, it is very important that the proteins of the diet have a high biological value.

TABLE V

SHOWING THE EFFECT ON THE GROWTH OF THE NURSING YOUNG OF DIFFERENT QUALITY OF PROTEIN IN THE MOTHER'S DIET.

No. of Experiment	*Wt. of Mother After Birth of Young. Grams.*	*Wt. of Mother 10 to 22 Days Later.*		*Wt. of Mother at End of Nursing.*		*No. of Young.*	*Weight of Young at Different Ages.*					
		Days.	*Grams.*	*Days.*	*Grams.*		*Days.*	*Grams.*	*Days.*	*Grams.*	*Days.*	*Grams.*
2369 *	144	18	150	46	120	4	18	71	31	107	46	123
2069 †	215	10	232	22	205	4	10	100	22	197	..	...
2370 ‡	192	12	170	37	170	5	12	74	33	160	37	175
2153 §	175	15	182	28	192	5	15	137	28	277	..	...
2365 ‖	173	18	157	45	146	5	18	70	30	102	45	210
2186 ¶	212	22	195	33	195	6	14	125	22	184	33	280
2767 **	270	19	275	29	270	6	19	163	29	330	..	...
2370 ‡	177	20	145	44	175	7	12	81	33	167	44	250
1236 ‡‡	142	..	...	40	146	7	16	133	30	286	40	544
2186 §§	215	17	213	45	215	9	11	123	17	153	45	382
2811 ‖‖	205	19	225	28	215	10	19	225	28	387	..	...

* Diet contained 9 per cent of protein from maize and peas. (Formula on p. 114.)
† Diet consisted of milled cereal products, legume seeds, beefsteak, a salt mixture and cabbage. (Formula p. 114.)
‡ Diet contained 9 per cent of protein from wheat and peas. (Formula p. 114.)
§ Diet derived its protein from milled cereals, beefsteak and legume seeds. (Formula p. 114.)
‖ Diet derived its 9 per cent of protein from barley and navy beans. (Formula p. 114.)
¶ Diet contained 9 per cent of protein derived from wheat and beefsteak. (Formula p. 114.)
** Diet derived its protein from whole cereal grains, legume seeds and casein. (Formula p. 114.)
‡‡ A high protein diet in which the protein was furnished by 50 per cent of beefsteak. This was supplemented so as to make good all its dietary deficiencies. Note the rapid and vigorous growth of the young. The formula for this diet is given on p. 114.
§§ Diet contained 9 per cent of protein derived from wheat and beefsteak. Although the protein content was low, the quality was so high that the young made remarkable growth. (Formula of diet, p. 114.)
‖‖ Diet contained a liberal amount of protein derived from cereal grains, legume seeds, casein and milk. Note the remarkable growth of the young during the nursing period. (Formula of diet, p. 114.)

TABLE VI
Composition of Diets Described in Table V

No. of Exp.	Wheat, Grams.	Maize, Grams.	Barley, Grams.	Rolled Oat, Grams.	Bolted Wheat Flour, Grams.	Corn Meal,* Grams.	Rice, Grams.	Pea, Grams.	Navy Bean, Grams.	Beefsteak, Grams.	Cabbage,† Grams.	Dextrin, Grams.	NaCl, Grams.	$CaCO_3$, Grams.	Butter Fat, Grams.	Casein, Grams.	Milk Powder,‖ Grams.	Cod Liver Oil, Grams.
2369		60.0						13.6				20.9	1.0	1.5	3.0			
2069				8.0	30.0	15.5	8.0	8.0	8.0	10.0	10.0		1.0	1.5				
2370	60.0							13.6				20.9	1.0	1.5	3.0			
2153				9.5	30.0	19.5	9.5	9.5	9.5	10.0			1.0	1.5				
2365			50.0						13.6			30.9	1.0	1.5	3.0			
2186	60.0									4.1		30.4	1.0	1.5	3.0			
2767	30.0	19.5		9.5			9.5	9.5	9.5				1.0	0.5		10.0		1.0
2370	60.0							13.6				20.9	1.0	1.5	3.0			
1236 ‡										50.0		43.5	1.0	1.5	3.0			
2186	60.0									4.1		30.4	1.0	1.5	3.0			
2811	25.0	11.5		9.5			9.5	9.5	9.5				1.0	1.5	3.0		10.0	

* Degerminated corn meal.
† Cabbage desiccated, steamed and dried.
‡ Contained 1.0 per cent of KCl.
‖ Merrill-Soule Company's "Klim."

TABLE VII

Supplementary Relations Between Proteins from Different Sources.

All diets contained 9 per cent of protein, two-thirds of which was derived from the vegetable, and one-third from the animal tissue or from milk.

No. of Experiment.	*Sources of Protein.*	*Observations on Growth, Fertility, Infant Mortality.*
2193	Wheat 60, kidney 4.2 per cent.	Growth excellent; reproduction good; infant mortality low.
2191	Navy beans 27.2, kidney 4.2 per cent.	Growth fair; far superior to growth on 9 per cent of bean protein.
2179	Wheat 60, liver 4.1 per cent.	Growth good; high fertility but very high infant mortality.
2177	Navy beans 27.2, liver 4.1 per cent.	Same as Lot 2191.
2182	Rye 50, liver 4.1 per cent.	Growth excellent; fertility good; infant mortality high.
2176	Peas 27.2, liver 4.1 per cent.	Growth fair; far superior to that on 9 per cent of pea protein.
2181	Oats 40, liver 4.1 per cent.	Growth good; infant mortality high.
2188	Oats 40, beef muscle 4.1 per cent.	Growth not so satisfactory as Lot 2181; fertility good; infant mortality 100 per cent.
2189	Rye 50, beef muscle 4.1 per cent.	Growth good; about like Lot 2182; fertility good; infant mortality high.
2186	Wheat 60, beef muscle 4.1 per cent.	Growth excellent; reproduction good; infant mortality high.
2387	Oats 40, milk powder 9.3 per cent.	Growth good; inferior to Lot 2181; similar to Lots 2188; fertility good; infant mortality high.
2391	Barley 50, milk powder 9.3 per cent.	Growth fair; inferior to barley and liver, kidney or muscle.
2389	Soy bean 16.6, milk powder 9.3 per cent.	Similar to results with rations of soy beans with animal tissues.
2390	Peas 27.2, milk powder 9.3 per cent.	Similar to Lot 2176; results same as with peas with kidney or beef muscle.
2384	Wheat 60, milk powder 9.3 per cent.	Results not so good as with wheat with animal tissues.

The proteins of seeds are supplemented and enhanced better by animal tissues (meats) than by milk proteins. In all cases milk proteins enhance the proteins of seeds, however, and milk has the advantage of greater superiority as a supplement in respect to inorganic elements and is far superior to muscle meats as a source of fat-soluble A. (For further details see Charts showing growth curves.)

furnished two-thirds of the total protein and the animal tissue the remainder. Barley and milk proteins likewise proved inferior to barley and animal tissue proteins. Wheat and milk, while very good as a source of proteins when combined in the proportions adhered to in these experiments, was inferior to combinations of wheat and animal tissues. Soy bean or pea proteins appeared to be about as well enhanced by milk proteins as by the three animal tissues studied.

117. **The Problem of Estimating the Value of Any Diet Is a Complicated One.**—These observations, together with the data presented in another chapter showing the profound damage resulting from lack of sufficient of the essential mineral elements or of the three well established vitamins, illustrate how complicated is the problem of interpreting quality in a diet. One can never safely focus the attention upon a single factor and use this as a criterion of much significance. A great deal of detailed knowledge, both of the chemistry of food-stuffs and also of the nutritive needs of the body, is essential to the formation of safe judgments regarding any problem in nutrition.

Holding in mind the data presented in this chapter, one is naturally inclined to turn one's thoughts to the studies in experimental nutrition which have been conducted upon human subjects, and to evaluate them anew in the light of newer observations on animals. Conspicuous among nutrition studies on man are those of Chittenden (11) and of Benedict (12). Since far-reaching deductions have been drawn from these results a few words of comment are called for in reference to their trustworthiness as a basis of guidance in deciding upon a safe dietary regimen for man.

118. **Chittenden's Experiments with Low Protein Dietaries.**—Chittenden conceived the idea that a low protein dietary, when it is derived from a suitable variety of wholesome foods, will best meet the nutritive requirements of the body. He emphasized the logic of relieving the organs of the task of degrading daily more protein than is necessary for the repair of tissue waste. He also emphasized the fact that the body does not tend to store protein which is ingested in excess of the daily need, and that an excessive protein ingestion promotes putrefactive decomposition in the intestine, and results in the absorption of products which are physiological abominations. The logical deduction from this reasoning was that the protein intake should

TABLE VIII

Composition of Rations Described in Table VII

No. of Exp.	Wheat Grams.	Oats Grams.	Rye Grams.	Barley Grams.	Navy Bean Grams.	Soy Bean Grams.	Pea Grams.	Kidney Grams.	Liver Grams.	Beef Muscle Grams.	Milk * Powder Grams.	Dextrin Grams.	NaCl Grams.	$CaCO_3$ Grams.	Butter Fat Grams.
2193	60.0							4.2				30.3	1.0	1.5	3.0
2191					27.2			4.2				63.1	1.0	1.5	3.0
2179	60.0								4.1			30.4	1.0	1.5	3.0
2177					27.2				4.1			63.2	1.0	1.5	3.0
2182			50.0						4.1			40.4	1.0	1.5	3.0
2176							27.2		4.1			63.2	1.0	1.5	3.0
2181		40.0							4.1			50.4	1.0	1.5	3.0
2188		40.0								4.1		50.4	1.0	1.5	3.0
2189			50.0							4.1		40.4	1.0	1.5	3.0
2186	60.0									4.1		30.4	1.0	1.5	3.0
2387		40.0									9.3	45.2	1.0	1.5	3.0
2391				50.0							9.3	35.2	1.0	1.5	3.0
2389						16.6					9.3	68.6	1.0	1.5	3.0
2390							27.2				9.3	58.0	1.0	1.5	3.0
2384	60.0										9.3	25.2	1.0	1.5	3.0

* Half skimmed milk powder. Merrill-Soule Company's "Klim."

TABLE IX

SUPPLEMENTARY RELATIONS BETWEEN PROTEINS FROM DIFFERENT SOURCES. (VEGETABLE PROTEINS ONLY.)

ALL DIETS CONTAINED 9 PER CENT OF PROTEIN. TWO-THIRDS OF THE PROTEIN WAS DERIVED FROM THE FIRST NAMED, AND ONE-THIRD FROM THE LAST NAMED FOOD-STUFF, EXCEPT LOTS 2346, 2344 AND 2345 IN WHICH EACH GRAIN FURNISHED HALF THE TOTAL PROTEIN.

No. of Experiment.	*Source of Protein.*	*Observations on Growth, Fertility and Infant Mortality.*
2367	Peas 27.2, Navy beans 13.6 per cent.	Very slow growth; permanent stunting. True of all combinations with legume seeds.
2383	Navy beans 27.2, soy beans 8.3 per cent.	Same as Lot 2367.
2346	Wheat 45, rolled oats 30 per cent.	Good growth; fertility low; long nursing periods; young inferior.
2344	Wheat 45, maize 45 per cent.	Growth fair; not so good as Lot 2346. Fertility low and nursing period long. Young inferior.
2345	Maize 45, oats 30 per cent.	Growth about like Lot 2346. Fertility high and infant mortality high.
2381	Barley 50, soy beans 8.3 per cent.	Good growth; fertility low; young inferior.
2378	Wheat 60, soy beans 8.3 per cent.	Same as Lot 2381.
2365	Barley 50, navy beans 13.6 per cent.	Good growth; fertility good; long nursing periods; infant mortality high.
2380	Oats 40, soy beans 8.3 per cent.	Fair growth; not so good as Lot 2381; fertility low.
2369	Maize 60, peas 13.6 per cent.	Fair growth; not nearly so good as Lot 2370. Fertility low. Nursing periods long. Young inferior.
2372	Oats 40, peas 13.6 per cent.	Good growth; much better than Lot 2369. Not so good as Lot 2370. Nursing periods long. Mortality high.
2370	Wheat 60, peas 13.6 per cent.	Very good growth; fertility good; infant mortality quite high. Nursing periods long. This combination is the best of all cereal and legume mixtures studied.

Cereal grains enhance each other's proteins better in all cases than do combinations of proteins of two legume seeds. Neither of the above are equal in the quality of their proteins to certain combinations of a legume seed with a cereal in which the cereal furnishes two-thirds and the legume seed one-third of the total protein diet.

In Tables VII and IX the diets were satisfactorily constituted with respect to all factors other than proteins, so the results of the experiments described turned entirely on the biological value of the proteins of the rations. The formulas for the rations used in these experiments are given in full on pages 117 and 119.

TABLE X

COMPOSITION OF THE DIETS DESCRIBED IN TABLE IX

No. of Experiment.	Wheat grams.	Maize grams.	Oats grams.	Barley grams.	Peas grams.	Navy Beans grams.	Soy Beans grams.	NaCl grams.	$CaCO_3$ grams.	Dextrin grams.	Butter Fat grams.
2367					27.2	13.6		1.0	1.5	53.7	3.0
2383						27.2	8.3	1.0	1.5	59.0	3.0
2346	45.0		30.0					1.0	1.5	20.5	3.0
2344	45.0	45.0						1.0	1.5	5.5	2.0
2345		45.0	30.0					1.0	1.5	20.5	2.0
2381				50.0			8.3	1.0	1.5	36.2	3.0
2378	60.0						8.3	1.0	1.5	26.2	3.0
2365				50.0		13.6		1.0	1.5	30.9	3.0
2380			40.0				8.3	1.0	1.5	46.2	3.0
2369		60.0			13.6			1.0	1.5	20.9	3.0
2372			40.0		13.6			1.0	1.5	40.9	3.0
2370	60.0				13.6			1.0	1.5	20.9	3.0

be reduced to as low a level as will serve to keep the body in nitrogen or protein equilibrium.

In order to demonstrate whether such a regimen is safe for the adult Chittenden tested upon himself the proposition which had hitherto been accepted on the authority of Voit and of Atwater, that the average adult at medium work requires about 116-120 grams of protein per day. He was able to reduce his protein intake to about one-third this amount and as a result felt better and was clearer mentally than he had been on a more liberal protein dietary. A brief comment has already been given of the experimental demonstration which he planned and carried out during 1903-04 at Yale University, in which a group of faculty men, a group of students and a group of soldiers participated. During a period of nine months while this study was going on the men reduced their protein intake to about half the accepted standard requirements. There was no evidence that these men were not in excellent physical condition at the end of the period of observation, and the deduction was drawn that such a dietary regimen appeared for an indefinite period to be suitable for the maintenance of physiological well-being in the adult.

Reference has also been made to the experiments of F. G. Benedict, which covered the period of a school year, the experimental subjects being a college group of volunteer students. This investigator was led to abandon his earlier view that a liberal protein dietary best serves the promotion of physical health, and to conclude that his experience with young men restricted for a few months to an abstemious diet low in protein warranted the acceptance of the dietary principles enunciated by Chittenden.

119. **Animal Experiments Indicate That Liberal Protein Intake Best Promotes Health.**—The systematic and very extensive nutrition studies on animals during recent years, seem to place in a new light the older literature relating to human nutrition. There is no instance in our experience where a diet satisfactory in all other respects, but supplying just sufficient protein of good quality to support growth at approximately the maximum rate to the full adult size, has been found to promote as satisfactory nutrition over the entire span of adult life as would the same diet containing a more liberal supply of the protein factor. It has been frequently assumed by students and teachers of nutrition that after growth has been attained the

nutritive needs of the body for protein food can safely be met by a dietary regimen in which the protein content is lower than is essential for optimal growth. Of the numerous experimental data from the work of McCollum and Simmonds, none support this view. Rather do they all point to the conclusion that when the life history of the individual is considered, a generous protein ingestion or one allowing a fair margin of safety over the lowest percentage which just suffices to induce maximal growth in the young will serve to maintain optimal vigor for the longest possible period.

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Fig. 7.—The rations of these two rats had the same composition as shown by chemical analysis. They differed only in the source of the protein which they contained. The rat on the right grew up on a mixture of proteins from the corn kernel and wheat gluten; that on the left on a mixture of corn proteins and gelatin. The difference in size, and remarkable difference in appearance is solely the result of the difference in the quality of the proteins in the two diets. Corn proteins and gelatin do not supplement each other's amino-acid deficiencies. These animals were the same age when photographed, and had been confined for the same number of days to the experimental diets.

CHAPTER VI

THE DIETARY PROPERTIES OF INDIVIDUAL FOOD-STUFFS

120. **Results Obtained with the Biological Method for the Analysis of a Food-stuff.**—In preceding chapters an effort has been made to give what we actually know about what constitutes in chemical terms a satisfactory diet, and the type of experimental procedure by means of which this knowledge was gained. For the purpose of placing this knowledge in proper perspective and correlating it with the older views of problems in nutrition a brief account of certain earlier investigations and the deductions made therefrom were presented. With the object of broadening the vision of the present day investigators so as to enable them and their successors in this field to appreciate how carefully experimental work must be planned and controlled in order to avoid conclusions which tend to confuse rather than clarify, a critical examination of the technic of experimental methods has been included.

It will be appreciated how confusing was the task of interpreting the cause of failure or success with experimental diets, when it is recalled that a few years ago no definite conception was possible of the existence of at least three dietary factors which are indispensable in the food supply of man or certain animals. Fortunately for students in this field the rat requires but two of these, and this species therefore assumes special value, in gaining a satisfactory working hypothesis regarding the number of essential factors in its nutrition. Even with this species, however, in addition to the two unknown factors there were two variables, either of which might determine success or failure in the development of this species. These were the quality of the proteins, and the amounts of certain mineral elements contained in the food mixture. The solution of such a problem demanded first the accumulation of a considerable amount of data based upon the outcome of a series of experiments, each of which was not possible of interpretation except in the light of all the others. It must be admitted that success was actually in no small measure

the result of active imagination and successful theorizing as to the true meaning of the effects of the experimental diets on the animals observed.

In order to understand how foods should be combined so as to make good each other's deficiencies, it is necessary to describe the dietary properties of each of the more important natural foods. This will form the subject of the present chapter.

121. **Wheat.**—This is the most important seed grain used as food by all western peoples, and is second only to rice in respect to the quantity used as food for man. The latter is in greatest favor among peoples of the eastern hemisphere. The dietary properties of the wheat kernel have been described in Chapter II in connection with the development of the biological method for the analysis of a food-stuff. The proteins of this grain are about as efficient for the promotion of growth as are the same amounts of protein from milk or eggs, or of certain combinations of two or more foods whose proteins are so constituted as to supplement each other's deficiencies. There is no cereal grain yet adequately studied which has been found to contain proteins superior to those of wheat. Its prominent place in the diet of mankind is, therefore, justified by the results of experiments on animals. When the wheat kernel is satisfactorily supplemented with respect to all other dietary factors, its proteins have proven satisfactory for the promotion of ordinary growth and the maintenance of good nutrition over a considerable fraction of the normal span of life of the rat, even when the protein content of the food mixture did not exceed 9 per cent of its calorific value. This is illustrated by the records in Chart 4. The results of feeding diets in which wheat was the sole source of protein have not been uniformly successful, and it appears that some samples of wheat are superior to others. It is well known that the quality of the proteins vary markedly in different samples of wheat, with respect to their glutinous property so important in bread-making, and the reason for this seems not to have been satisfactorily explained. It may be due in part at least to variability in the proportions among the several individual proteins in the seed. If this is true, it would account for such inequalities in nutritional value as have been observed.

Wheat is too poor in calcium to meet the needs of the growing rat. The average content of this element per 100 grams of this cereal is about 0.041 gram. The optimum content of calcium for the growing rat is not far from 0.64 per cent of the

food mixture. Phosphorus, sodium, chlorin and iodin are also present in the wheat kernel in amounts too low to support normal nutrition in this species. The content of mineral elements in any plant product is subject to some variation, depending upon several factors, chief among which is the content of each of the several inorganic ions in the soil. The amount of water transpired during the growth of the plant is also a controlling factor (1).

In general the entire wheat kernel is not used as human food, and the grain is fed to animals only under exceptional circumstances, because it is usually more valuable for the manufacture of flour. Bread made from whole wheat is dark in color, but has a flavor which is very agreeable. Whole wheat flour does not possess very good keeping qualities. The germ of the seed (wheat embryo) is rich in oil, and this tends to become rancid when the kernel is broken by milling. The rancidity spoils the flavor of the flour. Furthermore, the insects which infest cereals select the germ as the site for the deposition of their eggs, so that whole wheat flour contains many more insect eggs than does flour free from germ.

122. **Wheat Germ.**—This constitutes but 1.5 per cent of the entire kernel. It contains more than 35 per cent of protein. Bran forms about 15 per cent of the kernel and contains 17-19 per cent of protein. The remainder of the seed, about 83 per cent, is endosperm, containing about 11 per cent of protein.

Wheat germ has dietary properties exceptionally valuable in several respects (2). Its proteins are abundant and are of good quality; its content of the essential mineral elements is much greater than in bolted flour; it is exceptionally rich in the anti-neuritic substance, water-soluble B, and contains a considerable amount of fat-soluble A. Probably enough of the latter substance is present to meet the needs of the growing rat if germ constituted about 75 per cent of the diet. Strange to say, it contains but very little of the anti-scorbutic substance, water-soluble C (3). The oil, of which the germ contains about 10 per cent, leaves a somewhat unpleasant after taste, and is somewhat injurious to animals (4).

The germ contains a yellow pigment in considerable amount and this contributes to the color of whole wheat flour. The color of the latter is, however, due principally to the bran layer. In order to make flour white, it is necessary to remove both the germ and the bran. The germ is plastic and can be removed in the

form of a large flake if the kernel is broken by a series of blows instead of by the old time grinding process for making flour. This is accomplished in modern milling by the roller process in which the kernels are broken by passing between rollers so set as to crush them. This method for reducing the wheat grain to a powder leaves the bran in large flakes which can be separated from the fine flour and the germ by mechanical processes. The part which goes to make bolted flour is that which is readily crushed by the rollers to a fine powder. It is separated from the low grade flour by passing through bolting cloth. The low grade flour, so-called, is made up to a great extent of the same parts of the kernel as the high grade or white flour, but contains in addition numerous very small flakes of bran with particles of flour attached thereto.

For some reason or other wheat germ as a stock feed has never found favor with farmers, and in recent times no effort has been made to market the pure product for feeding purposes. It is mixed with bran or a low grade flour known as middlings, and reaches the feeder in this mixed form. This is apparently the best use to make of it. Through private correspondence the author has been informed that a few persons, in districts not far removed from the milling centers, have employed wheat germ as a breakfast cereal. Its tendency to rancidity and to become infested with insects would prohibit its being marketed in the same manner as breakfast cereals in general. For the same reason it appears that the logical use of this product is the one now in vogue, since the great centers of the milling industry are near the great stock-producing areas.

123. **Bolted Wheat Flour.**—In point of quantity consumed, white flour is the most important article of diet of the American people, and is widely used in Europe. This is remarkable because it is notably deficient in more dietary factors than any other single food which enters in a large way into the diet of man, except sugars, starches and fats which are marketed in the pure state. Muscle meats are, however, almost in the same class. Bolted flour consists essentially of starch, proteins and inorganic salts. Its proteins are of relatively poor quality, and its mineral components are conspicuously lacking in calcium, sodium, chlorin, iron and phosphorus, some of the essential elements we regularly expect to find in satisfactory abundance in our foods (5).

The proteins of bolted flour are practically limited to two. These are called gliadin and glutenin, both of which are very

unlike any of the proteins in the animal body from the standpoint of their yield of the different amino-acids. These proteins are not constituted so as to enhance each other's value as food by compensating each other's deficiencies, and cannot, therefore, be effectively transformed into body proteins unless they are combined with other foods wisely chosen (6). Wheat flour is very deficient in all three of the recognized unidentified dietary essentials, fat-soluble A, water-soluble B and water-soluble C, the anti-ophthalmic, anti-neuritic and anti-scorbutic substances, respectively (7).

The merits of flour as a food rest essentially upon the peculiar glutinous properties of its proteins, which make possible the formation of dough. This is sufficiently tenacious to permit of leavening by the generation of carbon dioxid gas within it, through the agency of yeast or baking powder. By this means light spongy bread is secured, which has a pleasant flavor, and a texture which invites mastication. Bread and meat are the only foods which are prominent in the American diet which are chewed to any appreciable extent. Of these, bread is by far the most important in this respect. Bolted flour possesses still another virtue. It has excellent keeping qualities and can be distributed without commercial hazard over wide areas from the milling centers. This is a matter of great importance in a country like the United States. It will, despite its shortcomings from a dietary standpoint, remain our most important energy-yielding food.

It is not to be understood from what has been said that wheat flour is not a wholesome food. When properly combined with such other foods as make a well proportioned diet, every factor of which is so adjusted as to meet the needs of the body, it becomes an entirely satisfactory part of the diet. *The keynote to the discussion of the individual foods entering into the diet of man is the importance of using proper combinations of foods.*

124. **Bolted Wheat Flour Need Not Be Condemned Because of Its Deficiencies.**—The attitude which one should take toward the discussion of the relative merits of bolted as against whole wheat flour is now easy to understand and appreciate. The latter is decidedly more suitably constituted to maintain well-being for a short time if it serves as the sole article of diet, as it might under conditions approaching famine. Whole wheat flour is, however, a decidedly incomplete food, and needs to be *supplemented* with other foods in order to compensate for its

deficiencies. The unfortunate individual who through faulty habits of living, finds at an age at which he should be still in possession of the full vigor of middle life, that his efficiency is diminishing and the joy of living slipping away, has not infrequently turned for relief, to substituting whole wheat flour for the staple white variety. As a rule those who advocate this practice exhibit in some degree the spectral mien of the dyspeptic. They would gain much more through adhering to a diet well balanced than through clutching to this or any other dietary whim or fad.

Wheat bran has been studied by Osborne and Mendel (5). Their results indicate that the proteins of this part of the kernel have a higher value than those of the germ, and that they are distinctly superior to those of bolted flour. Their findings were not concordant, since but one rat in four succeeded in growing on their experimental diet. Bran is much poorer in water-soluble B than is the germ. They found 5 per cent of bran as the sole source of this factor to be entirely inadequate. McCollum, Simmonds and Pitz, have observed normal growth in young rats during five months with diets in which this substance was entirely derived from 2 per cent of germ, and Osborne and Mendel have also found 5 per cent of the latter to furnish sufficient water-soluble B (2).

No studies by means of biological methods have been made of the adequacy of the mineral content of bran, but one may judge fairly safely from the results of chemical analysis that it is too poor in calcium and probably also in sodium and chlorin. It contains but little of the factor, fat-soluble A. This statement is not made upon the results of a direct test, but on inference from the well-known fact that the entire wheat kernel is, like most seeds, well below the optimum in its content of this substance, for the amount contained in the kernel is in great measure located in the germ. Bran constitutes about 15 per cent of the entire kernel, and could not be expected to contain much of it.

125. **Maize Kernel.**—This cereal grain has dietary properties very similar to those of wheat. Its flavor and physical properties, however, are very different. Since its proteins have none of the glutinous properties it is not possible to form a dough with finely ground maize. In the Southern United States maize is much prized as a human food. It was found in a dietary study to constitute 23 per cent of the total food intake of Tennessee and Georgia mountaineers, and 32.5 per cent of that of Southern

negroes. Among 72 Northern families in comfortable circumstances only 1.6 per cent of the diet was derived from this grain (8). The great bulk of the maize crop, which in this country amounted to three billion bushels in 1917, is used in stock feeding.

The proteins of maize have a slightly lower value in nutrition when fed as the sole source of this dietary factor, than have those of wheat. Its mineral deficiencies are the same as those of the latter. These two grains are about comparable in their content of anti-neuritic substance, water-soluble B. It requires about 15 per cent of the food mixture of either, when they serve as the sole source of this factor, to enable young rats to grow in a normal manner. With such a diet, however, a female rat cannot successfully nourish four young during the nursing period, even when all other factors are highly satisfactory. For this purpose about half of the diet must be derived from a cereal grain, provided there is no other source of the anti-neuritic substance. Neither grain contains an appreciable amount of the anti-scorbutic substance, water-soluble C, unless it is germinated. During this process there is a rapid increase in their potency as foods protective against scurvy (9).

126. **Vitamin Content of Different Samples of the Same Food Varies Considerably.**—Much effort has been expended in recent years by a number of investigators, with a view to determining very accurately the vitamin content of different foods. It has seemed to McCollum and Simmonds, from the results of their studies, that this matter has excited greater interest than its importance justifies. They found in numerous comparative studies that different samples of cereal grains differ considerably in their content of water-soluble B. Steenbock's observations relative to the differences in fat-soluble A content of different samples of maize, is another evidence which supports the view that rather general statements as to the relative values of many of our common foods with respect to the uncharacterized dietary essentials is all that we can profitably seek to make on the basis of experimental tests. We are already in possession of about all the specific information in this field that we can make practical use of. The fact, that we can readily prepare diets from ordinary wholesome foods which will contain at least three to five times the minimum amounts of vitamins on which apparently normal nutrition can be maintained over long periods, tends to render the discussions, which one so frequently sees nowadays

about the advisability of taking concentrated commercial preparations of vitamins, a purely academic one, and based upon fallacious reasoning and lack of clarity of vision or of familiarity with existing literature describing experimental data.

127. **Fat-Soluble A Content of Yellow and Other Varieties of Maize.**—Steenbock and Boutwell (10) observed that yellow maize is far superior to white or red varieties as a source of fat-soluble A. They believed at one time that the fat-soluble A is in general associated with the yellow pigment of plants. This view has been in great measure discarded.

Maize which is used as human food is now freed from its germ and its bran layer in a manner analogous to wheat, and also for the purpose of improving its appearance and more especially its keeping qualities. Maize germ, like wheat germ, is rich in oil and this tends to become rancid when the kernel is ground and exposed to the air. Meal which contains the germ is more liable to harbor insects when kept over a period of warm weather, than is ordinary corn meal. Both white and yellow grain is used for making meal for human consumption. The former is in greatest general favor with the public because it has been educated to a liking for white flour and white rice. Corn oil is now marketed as a salad oil.

128. **Oats.**—Rolled oats are used in America in human nutrition principally as a breakfast food. Oats have long been a principal food grain in Scotland. The oat kernel is comparable with wheat or maize in its dietary properties in nearly all respects. It appears from the data available that there is distinctly less fat-soluble A in rolled oats than in wheat and certainly much less than in yellow maize. There is no demonstrable amount of anti-scorbutic substance in the oat kernel.

Oats have been a great favorite among feeders of horses, and are believed by many to have exceptionally high nutritive value because animals fed liberally with oats frequently show much spirit when driven or ridden. In the experience of McCollum and Simmonds, rats which are fed on restricted diets of certain types, faulty in one or more respects, become restless, irritable and apprehensive, and the thought occurs that perhaps the common expression among horsemen that an animal "feels his oats" may have been misinterpreted. The tendency of horses fed liberally on this grain to exert themselves greatly without urging may be the result of increased irritability and apprehensiveness.

129. **Rice.**—This is the most important cereal grain in the diet of more than half of the human race, especially that portion

of the race in Asia and the islands of the Pacific, and is used to a considerable extent throughout the world. It has never found much favor in the United States, but is used in small amounts. Among primitive peoples rice is eaten without polishing, in which form it is known as red rice, but it is ordinarily so treated as to lose a large part of its germ. This loss results from the pounding of the kernels in rude mortars in which process the germ is separated from many of the kernels and lost in subsequent handling. The bran layer, which is richer in mineral salts than the endosperm of the seed, is retained in this process.

Rice which is used for export and for sale in the large cities at some distance from the place of production, is polished by stirring the kernels. The abrasive action results in wearing away the bran. The germ is in an exposed position and easily rubs off in this process and is, therefore, left with the bran. This mixture is known as rice polishings. The germ of rice, like that of wheat or maize, consists of cellular structures which are the seat of protoplasmic activity, and is a more complete food than any other part of the kernel. It contains almost all the fats found in the grain, and is more efficient in nourishing insects as well as higher animals than is the polished grain. Unpolished rice loses its flavor owing to the fats becoming rancid, when kept for considerable periods in a warm climate, whereas the polished kernel can be handled without commercial hazard because it contains almost no fat and does not support the growth of insect larvæ.

The practice of polishing rice had its origin in the desire to improve its keeping quality, and the incidental whitening of the kernels has led to the establishment of a demand for a white product. *This, and the artificially established liking for white flour and white corn meal, is an illustration of the failure of the instinct of man to serve as a safe guide in the selection of food.* The esthetic sense is appealed to in greatest measure in this case by the products of lowest biologic values.

Attractiveness of rice to the eye is so important a factor commercially that the practice of artificial whitening of the polished kernels has come into vogue. This is accomplished by coating the kernels with talcum powder, the latter adhering by means of a thin coating of glucose. The milky appearance of the water in which rice is washed, is due to the talcum remaining for a time in suspension. Rice which has been polished but not coated in this way is called brown rice as contrasted with the coated or white rice.

Chart 3 shows that there are four dietary factors in which

polished rice is of such poor quality as to require improvement before it becomes a complete food. Its proteins like those of other cereal grains are of low biological value, and need to be enhanced by the addition of other proteins which are so constituted as to have a supplementary relationship to rice proteins (11). It is entirely too poor in all essential mineral elements to meet the needs of a growing animal, and is nearly free from both fat-soluble A and water-soluble B. The experimental data in Chart 3 was obtained with the rat and does not bring out the fact that rice is lacking in the anti-scorbutic substance. This substance is not essential in the diet of the rat for the reason that this animal is able to synthesize the complex, whereas man, monkey and guinea pig must secure their supply from the food. This point will be further discussed in Chapter VIII in connection with the deficiency disease scurvy.

130. **Barley and Rye.**—These and apparently other cereal grains possess essentially the same dietary properties and shortcomings as do those already described. Experiments with animals have shown that they must be improved in respect to the same factors in order to make them complete foods (12).

131. **Peas and Beans.**—These are seeds belonging to a class of plants known as legumes, which are able to utilize the nitrogen of the air for the purpose of synthesizing proteins during growth. Other plants have to secure their nitrogen from the soil in the form of nitrates or ammonium compounds. The legume seeds are much richer in protein than are any of the cereal grains. Wheat, maize, oat, and rice kernels contain about 11, 10, 15 and 9 per cent of protein, respectively, whereas peas and beans contain about 23 per cent. For this reason the latter seeds have long been regarded as especially valuable from the standpoint of protein content. Beans have been frequently spoken of as the "poor man's meat." Unfortunately modern experimental studies have not lent support to this view. Their proteins appear from the results of chemical analysis, to be much more adequately constituted than are those of wheat or maize, but nutrition experiments on animals show clearly that there is something lacking in their molecules which limits the extent to which they can be converted in the body into tissue proteins. The nature of the limiting factor has not been determined (13).

132. **Osborne and Mendel's Studies on Legume Proteins.**—Osborne and Mendel (14) were unable to secure any growth with pea and bean proteins when these were carefully purified and

fed as the principal source of nitrogen in the diet, the proteins of the legume seeds being supplemented only with the nitrogen of "protein-free milk." It has been shown in McCollum's laboratory that the protein mixture contained in the entire seed of the pea or bean is complete and can support fair growth when they serve as the sole source of protein in the diet. The other deficiencies in the seeds must, of course, be made good. Growth is possible only when the intake of protein in such diets is rather high (13). The proteins of these seeds are distinctly poorer in quality than are the combinations of proteins found in each of the cereal grains. Beans contain considerable amounts of hemicelluloses which are not digestible but easily fermented in the intestine with the formation of gas and frequently cause flatulence.

A matter of great importance in comparing the relative values of the proteins of the legume seeds with those of meats, is the extent to which each supplies an abundance of those particular amino-acids which are not yielded in optimal amounts by the proteins of the cereal grains and tubers. The cereals form, in temperate climates, the greater fraction of our foods and supply most of the protein and energy of the diet. The milled products of these contain proteins of relatively low value and are deficient, without exception, in certain amino-acids. They may, when combined, mutually improve each other to a certain extent, but there are some essential amino-acids which are not abundant even in mixtures of several grains. In looking toward improvement of a dietary consisting largely of milled cereal products one of the important factors is the enhancement of the protein content. It is not so important to secure a high intake of protein as to have proteins of excellent quality. Relatively small additions of the right kind of protein greatly enhance the value of the proteins of cereals.

133. **Soy Beans.**—The soy beans have long been an important article of diet among the Chinese and Japanese peoples, and have been grown within recent years somewhat extensively in the United States. The dietary properties of this seed have been studied in several laboratories (15). The results show that this seed belongs in the same class with peas and navy beans for it contains proteins which are adequate when fed at a plane corresponding to 17 per cent or more of the diet, and can support growth when they form the sole protein supply.

When soy beans are supplemented with potassium and calcium salts and butter fat (fat-soluble A) the nutrition of rats was

markedly improved as shown by better growth, larger litters, better developed young and lower mortality of the latter.

134. **Peanut.**—The peanut is a legume seed which is not only eaten in considerable quantities at times other than meal-time in the roasted state, but is extensively converted into peanut butter in which form it is eaten with bread. Peanuts are grown extensively in the South for feeding hogs, but if fed too liberally they produce oily pork. To avoid this condition the animals are frequently finished on some other feed before being sent to slaughter.

Daniels and Loughlin (16) have conducted feeding experiments with Spanish peanuts. Their results show that they have the dietary properties common to seeds, and that they have no marked peculiarities. Their greatest deficiencies lie in their mineral content, and in fat-soluble A. Johns and Jones (17) have shown that the proteins of the peanut are unusually rich in lysin.

135. **Cotton-seed Flour.**—This is a product which is prepared from the cotton seed. In its manufacture the oil, hull and a considerable amount of resinous substances are removed. This flour has a nutty flavor and an effort has been made to promote it as a human food. Its dietary properties have been studied by Richardson and Green (18) and by Osborne and Mendel (19). The results show that like all other seeds, the proteins are complete when fed in the mixture in which they occur in the seed, and that the deficiencies of the product are those common to seeds, lack of sufficient calcium, sodium, chlorin, probably also of phosphorus and fat-soluble A. The proteins of this flour are of such nature that they supplement the deficiencies of those of maize gluten, a commercial product obtained in the manufacture of corn starch (20). For this purpose they are equal to the proteins of brewer's grains, but inferior to lactalbumin.

136. **Cotton-seed Products Contain the Poisonous Substance Gossypol.**—Cotton seed, and the press cake obtained in the manufacture of cotton-seed oil, contains a poisonous substance to which Withers and Carruth gave the name *gossypol* (21). The oil extracted from the seed either by pressing or by extraction with fat solvents is also toxic to animals because of the presence of this principle. Cooking of the meal or heating in the hot press method for extracting the oil causes a change in this substance which renders it no longer soluble in oil or ether. It therefore remains in the meal (22). While cotton-seed flour or meal is a valuable feeding-stuff in animal production, its

use as a human food is not to be recommended because no assurance is yet offered that the toxicity of the products can be removed entirely. The same may be said of cotton-seed flour. It must be further studied before it can be recommended as human food.

137. **The Leafy Parts of Plants.**—These have dietary properties very different from the seeds. The contrast between the state of nutrition which can be secured in omnivorous animals with suitable mixtures of leaf and seed, as against mixtures of seeds alone, even in complex combinations, was first pointed out by McCollum, Simmonds and Pitz (23). It has not been found possible to secure satisfactory growth, or prolonged well-being in animals fed exclusively on seeds and seed products. The first leaf which was studied was that of the alfalfa plant, for the reason that the immature leaf in a finely ground form is available as a commercial product known as alfalfa flour.

The dietary properties of mixtures of leaf and seed are well illustrated by a series of nutrition experiments carried out with mixtures of seed 60 per cent and alfalfa leaf 40 per cent. The seeds employed included wheat, maize, rolled oat, rice, pea and navy bean. The degree of success in inducing growth with these simple mixtures of one kind of seed with one kind of leaf is much greater than can ever be secured with even such diets as a combination of wheat, maize, oat, hemp seed and millet seed in equal proportions. The latter mixture can support a fair amount of growth when its inorganic deficiencies are corrected, but without additions of mineral salts almost no growth can be secured. Chart 7 shows typical growth records of animals confined to diets of leaf and seed. Among the seeds studied, the oat kernel is best supplemented by the alfalfa leaf. A simple mixture of 60 per cent rolled oats and 40 per cent alfalfa leaf induces in the rat nearly normal growth to the full adult size. Animals grown on this diet have shown moderate fertility and fair success in the rearing of young. However, they were not nourished in the optimal manner, for they fell considerably below the maximum capacity of well nourished animals in respect to fertility and successful rearing of young.

An examination of the leaves of other plants showed that these can in a general way be classed together as food-stuffs of similar character, since they resemble one another more or less closely, just as the seeds resemble each other in their nutritive properties. From the dietary standpoint the leaf proves to be

a very different thing from the seed. The dry leaf usually contains from two to five times as much ash as does the seed, and is always especially rich in just those elements in which the seed is poorest, calcium, phosphorus, sodium and chlorin. It follows that the leaf supplements the inorganic deficiencies of the seed. The leaf contains in most cases much more of the dietary factor fat-soluble A than is found in any seed. The leaf as well as the seed contains protein, and amino-acids (24). The amount varies from 8 per cent of protein (N x 6.25) in such fleshy leaves as cabbage, after drying, to more than 15 per cent in dry alfalfa leaf, and clover leaf, to 30 per cent or more in the dry leaf of the turnip. In most cases, probably not all of the nitrogen in leaves is in the form of compounds which have a nutritive value, but the leaves appear, from the data available, to supplement the proteins of the seeds and to enhance to some extent their value. The leaf supplements all the deficiencies of the seed, but not necessarily in a highly satisfactory manner at all times.

138. **Differences in Function of Leaf and Seed as a Basis of Predicting Dietary Properties.**—It is interesting to reflect upon the reasons why the leaf of the plant should show such decided differences in its nutritive properties as contrasted with the seed. A consideration of the function of the two organs of the plant gives the clue to the cause. The seed is composed of a germ, which in most cases forms but a small part of the entire seed, together with a relatively large endosperm. The germ consists of living cells, which respire and which are capable of germination (multiplication) when the conditions are favorable. In the wheat kernel the germ constitutes but 1.5 per cent of the entire kernel. The endosperm, on the other hand, contains large amounts of reserve materials such as protein, starch, sugars, fats and mineral salts. These are not living matter but its by-products. The endosperm is, therefore, in most respects comparable to a mixture of purified food substances. Experiments have abundantly demonstrated that the endosperm contains relatively little of the anti-neuritic substance, whereas the germ is rich in this dietary factor. The last statement perhaps needs some qualification in the light of recent investigations. Osborne and Mendel (5) state that when they carefully dissected the germ from the wheat kernel, and secured practically pure germ substance, the product contained no water-soluble B. The latter substance is certainly situated immediately adjacent to the germ, for the germ as obtained in the milling process contains a very

large part of all that is found in the entire kernel. The dietary factor, fat-soluble A, is likewise largely localized in the germ, where it is relatively abundant as compared with other seed products. Since the germ in most cases forms such a small fraction of the seed, the seed itself is in general poor in this substance as compared with the leaf, which is in large proportion made up of vegetative tissue containing all the protoplasmic structures necessary for active metabolism.

The leaf of the plant, on the other hand, is rich in cells which during life are actively functioning, and which, with but few exceptions, contains but little reserve food material. It is the laboratory of the plant. The chlorophyll, its green pigment, enables it to utilize the energy of sunlight, and from the carbon dioxid absorbed from the air together with water and mineral salts derived from the soil, it builds up protein, starch, sugar and fat, which are used for the growth of new plant tissue, or for storage in the seed, tuber or other organ. The surface of the leaf is a mosaic of living cells. It contains all the complexes necessary for the nutrition of animal cells, and the leaf is qualitatively a complete food.

139. **Thin Leaves Are Better Than Thick Ones.**—From the dietary standpoint the quality of the leaf may vary to a considerable degree. Some leaves are thin, cellular structures which dry easily when separated from the stem. These have little reserve food material and relatively little inert tissue of a skeletal nature. Others, of which the cabbage is an example, have become modified as storage organs, and contain a considerable amount of reserve food comparable to that stored in the endosperm of the seed. The cabbage leaf also contains more than the average amount of cellulose and related substances which serves as supporting tissue. The dietary properties of such leaves are modified by these peculiarities since the cellular elements are diluted by the more inert tissues and reserve food substances in them. The less a leaf partakes of the function of a storage tissue, the more pronounced will be the leaf quality as a food. The fleshy leaves tend to have in some degree the dietary properties of the seed, and in this respect stand between the thin leaves and the seeds. In the case of the alfalfa leaf, which is a typical thin leaf of high nutritive value as a forage plant, the content of fat-soluble A has been stated by Steenbock to be greater than its content of water-soluble B (25).

140. **Tubers.**—The tubers of certain plants constitute, after

the seeds, one of the most important classes of energy-yielding foods. The white Irish potato is by far the most important of these in the temperate zones. In the Orient several kinds of tubers are widely used as human food. An examination of the potato has revealed the special dietary properties of this tuber to be just what we should expect from its function as a storage organ for reserve food in the plant (26). The function of the potato is two-fold, reproduction of the species and a source of food supply for the young potato plantlet while it is developing a root and leaf system, which make it independent of the food in the old tuber. The "eyes" of the potato represent groups of cells which are analogous to the germ of the seed. These are the locations from which the potato sprouts when the conditions are favorable. There is underneath the skin of the tuber a layer of cells which are alive and which respire during the life of the tuber. The interior of the potato consists almost entirely of water, starch, protein, and to some extent of mineral salts. The cellular structures in the interior are gorged with starch. This portion is therefore analogous to the endosperm of the seed. Both are comparable to a mixture of purified protein, carbohydrate and salts, which, as we have previously seen, are not capable of supporting life. This portion like the portion of the rice kernel remaining after polishing, is almost devoid of the dietary essentials, fat-soluble A and water-soluble B, and accordingly cannot meet the nutritive needs of an animal, even though it may have an appropriate chemical composition.

From the dietary standpoint the potato is to be classed with the seeds because it consists largely of reserve materials and of relatively little vegetative tissues. It is very likely that when it is steamed and the thin, paper-like skin removed without the loss of the cellular layer just underneath, it will contain relatively more fat-soluble A than certain of the cereal grains. Although it has not been subjected to experimental test, it is probable that a potato pared in the ordinary way and the parings discarded, is changed in its dietary properties in much the same manner as is the rice kernel during polishing. In the latter case the bran layer and the germ are both rubbed off, leaving the endosperm without the small quota of cellular elements it possessed in the natural state. The protein of the potato is not quite so valuable for the support of growth as is that of the cereal grains when it serves as the sole source of this dietary factor (26). It is when raw an excellent anti-scorbutic food.

141. There Is Some Evidence That Potato Nitrogen Is Exceptionally Valuable for "Repair."—There have been a number of experiments of short duration giving results which indicate that in the human subject the nitrogen of the potato is of extraordinary value for replacing that lost through daily catabolism in the adult (27). McCollum, Simmonds and Parsons (26) have tested this question by comparing with the protein of the cereal grains, the value of the nitrogen of the potato when this tuber was supplemented in such a manner as to make good all its dietary deficiencies, except protein. The experiments involved growth tests in the young rat. The results show beyond doubt that potato nitrogen falls considerably below the value for growth possessed by individual cereal grains, when each of these serves as the sole source of supply of the digestion products of protein.

The experiments which have been reported of the maintenance of rats on potato protein support the conclusion of Rose and Cooper (27), that this nitrogen has a high biological value for the replacement of the tissue substance lost in endogenous metabolism. This observation has a bearing on the question whether the processes of repair can be carried on with certain chemical complexes absent from the diet, which are essential when growth takes place involving the formation of new tissues.

142. Fleshy Roots.—These are in a general way similar to the potato with respect to the relation between dietary properties and biological function. The roots we employ as foods are those which are highly modified as storage organs, and resemble the potato in possessing a very high water and starch content and but very little protein. In the case of the sugar beet, the sugar replaces starch in a great measure. As in the potato there is a cellular layer at the periphery, but the interior is loaded with reserve food-stuffs. Appropriate feeding tests have shown that the properties of the beet resemble those of the seed and tuber rather than those of the leaf (28). The fleshy roots, the dasheen and sweet potato, have an inorganic content which resembles that of the seeds in a general way, so that an inspection of the analytical data relating to the composition of the ash of seeds, tubers and roots gave no promise that combinations in diets of seeds with either of the latter classes of food-stuffs would correct the inorganic deficiencies of the former. Feeding tests in which the seeds and tubers or roots have been combined and so supplemented with purified protein, and butter fat (fat-soluble A)

that all the deficiencies of the mixture except the inorganic were made good, have given interesting results. The mineral elements derived from the natural foods in the mixtures, are not furnished in proportions to meet the nutritive needs of a growing animal. It is the low content of calcium, phosphorus, sodium and chlorin which is responsible for the failure of the animals, for when these are added along with protein and fat-soluble A, growth proceeds in the normal trend.

In the dry state, therefore, the fleshy roots resemble the seeds in food value. There is, however, one difference which should be mentioned. Like the potato and unlike the seeds the fleshy roots contain a large part of their nitrogen in forms which are chemically much simpler than protein. A part of this nitrogen is actually in the forms of digestion products of protein, and these are of the same value as protein. This value depends entirely on the presence of a complete list of amino-acids necessary for the construction of body proteins, and on the proportions in which they occur. There is always a part of the nitrogen in the form of other complexes which have no nutritive value.

A study of the carrot has been made by the biological method by Denton and Kohman (29). Their results show that it was possible to maintain young rats for some weeks on a diet composed exclusively of carrots, supplemented with sodium chlorid and a calcium salt, but the animals were not able to grow. They found it necessary to supplement the protein, and augment the fat-soluble A content before the rat was able to maintain growth even in an approximately normal manner.

143. **Great Differences Are Found in the Fat-Soluble A Content of Different Kinds of Roots.**—Steenbock and Gross (28) have studied the more important fleshy roots used as food in the United States for man or animals, especially with respect to their content of fat-soluble A. They adopted the standard method of McCollum and Davis, feeding a purified food mixture supplemented with varying amounts of a natural food as a source of the dietary essential in question. Their results are of unusual interest for they showed that carrots and sweet potato, both of which contain much yellow pigment, are far better sources of fat-soluble A than are any of the roots which do not have a yellow color. Rutabega, dasheen, red beet, parsnip, potato, mangle and sugar beet appear from their results to contain practically none of this substance. They were inclined to the belief that this dietary essential is associated in foods with the yellow pigment.

This idea rested on insufficient evidence, as will be shown in Chapter XII, where the literature relating to this subject will be discussed. The roots so far as they have been studied, appear to be effective sources of water-soluble C.

144. **Fruits.**—From the results of chemical analysis fruits appear to be closely comparable in their composition to the familiar vegetables such as the tubers and roots. They all contain much water, and varying amounts of sugars, and are relatively insignificant as sources of protein or fat. They are much more attractive to the palate than are most of the vegetables. They enjoy the popular reputation of possessing mild laxative properties, and tend to increase elimination by virtue of their mild diuretic qualities, part of which are due to the extra water consumption, and part to the action of certain salts of organic acids they contain.

Fruit juices or the edible parts of fruits differ from the cereal grains, and resemble in a very important respect the vegetables, which are morphologically tubers or roots. There is an excess of basic radicles which renders their ash alkaline, whereas most seeds give an acid ash. Meats are also of acid character. The meat and bread portion of our diet, when oxidized in metabolism leads to the formation of an excess of acid over base-forming substances. It is now a well established fact that a certain alkali reserve in the blood is essential to maintain its capacity to carry carbon dioxid to the lungs for elimination, and that a common pathological condition, acidosis, exists in which this reserve falls below normal. This forms sound reason why the addition of fruits and vegetables to the diet tends to the establishment of a proper acid-base equilibrium in the various fluids of the body.

The fruits differ from the leafy vegetables in containing little calcium. They resemble the tubers and roots insofar as they do not tend to supplement the deficiencies of seed or meat products in this respect.

145. **Citrus Fruits Have Long Been Valued as Anti-scorbutic Foods.**—Certain fresh fruits, especially those of the citrus group, which includes the lemon, orange, lime and grapefruit, have long enjoyed popularity for their potency in preventing scurvy. This has been shown in recent investigations to be well founded and to depend upon the presence of a specific chemical substance, water-soluble C. Wide differences in the value of different fruits for this purpose have been shown by investigations

relating to scurvy. The content of the anti-neuritic substance, water-soluble B, of several fruits has been studied by Osborne and Mendel, and by Byfield, Daniels and Loughlin (30). Their findings indicate that the anti-neuritic value of orange juice is about the same as that of an equal volume of milk. Orange juice to the extent of 55 c.c. per 100 grams of food mixture was not sufficient to furnish the optimal amount of the factor B, but 75 c.c. seemed satisfactory. Lemon juice was comparable in this respect to orange juice. Ten c.c. of juice per day afforded sufficient water-soluble B to support growth at the normal rate when added to an otherwise adequate diet. Grapefruit was also found to contain the anti-neuritic, water-soluble B. McCollum and Simmonds have found orange juice to contain demonstrable amounts of fat-soluble A (31).

Commercial grape juice, and fresh apple juice were found inferior to the citrus fruits as a source of water-soluble B. Pears resemble apples in this respect, but prunes seemed superior to either. The fruit juices tested by Osborne and Mendel did not show appreciable amounts of fat-soluble A (30).

146. **The Banana.**—The banana has been studied as food for the rat by Benedict and Sugiura (32) and as a nutrient substance for the banana fly, *Drosophila ampelophila*, by Loeb and Northrup (33). The former investigators found it deficient in protein, and in water-soluble B. This last observation is remarkable since banana constituted about 80 per cent of their experimental diet. Their studies also seem to verify the generalization of Steenbock and Gross (28) that this yellow fruit contains more fat-soluble A than do fruits in general, or more than the roots and tubers not so pigmented. Benedict and Sugiura also stated that in their experience casein proved a much more effective supplement to the banana than washed and dialyzed beef. In their experiments the banana supplemented with casein, and a source of water-soluble B (yeast or carrot extract) proved inadequate for the production of milk by lactating rats. The failure lay in the quality of the milk and not in the quantity, since the mothers failed to succeed with both small and large litters.

Loeb and Northrup found sterile banana inadequate for the nutrition of the banana fly, but banana cultured with yeast was satisfactory (33). The interpretation placed upon this observation is that the yeast cell produces synthetically some substance or substances, not present in the banana, but necessary for the nutrition of the fly. The nature of this relationship between the

development of yeast and the improvement of the nutrition of this insect is not clear.

147. **Nuts.**—Nuts have not been extensively studied by the biological method. Little can be said of their dietary properties other than what can be deduced from their chemical composition and from their function in the plant from which they are derived (34). With the exception of the chestnut, nuts are very rich in protein, and fat, and poor in carbohydrates. The edible portions of several of the more highly prized nuts contain the following amounts of protein: Almond 21 per cent; beech-nut 22 per cent; brazil nut 17 per cent; chestnut 6.2 per cent; pecan 11 per cent; walnut 18.5 per cent. The fat content of these nuts is on an average: Almond 55 per cent; beech-nut 57 per cent; brazil nut 67 per cent; chestnut 6.2 per cent; pecan 71 per cent; walnut 64 per cent. The digestible carbohydrate of most nuts is very small. The chestnut is unique among the ordinary nuts in that it contains about 45 per cent of starch and but little fat. Feeding studies have shown that several nuts have essentially the same dietary properties as seeds in general (34).

The flavors of nuts are especially attractive, and they form a group of highly desirable food-stuffs. They are, however, the seeds of plants and one would predict that their dietary properties are not such as to make them effective supplements for the cereals, legume seeds, tubers, roots or fruits, except in respect to the protein factor. A diet composed of such combinations of food may be chemically balanced so far as analysis can show, but be decidedly defective in other respects.

148. **Animal Tissues.**—These include veal, chicken, beef, pork, lamb, etc. They must be differentiated into two groups, on the basis of whether they are glandular organs such as the liver and the kidney or highly specialized tissue such as the muscles or connective structures. It seems certain that we are justified in generalizing to the extent of saying that those organs which are the seat of metabolic activity of the type concerned with the elaboration of secretions or intermediate or end products of metabolism are more complete foods than are those characterized by inertness such as are the supporting and the contractile tissues. One would expect, in the light of the marked differences in the dietary properties of the vegetative parts of plants as contrasted with the storage tissues to find comparable differences in the nutritive value of animal tissues having different functions. Experiment has shown this to be warranted.

Watson (35) restricted birds to an exclusive diet of muscle meat, and observed profound pathological changes, especially nervous disturbances and paralysis (polyneuritis), hypertrophy of the thyroid gland to the extent of ten times its normal size, and hypertrophy of the parathyroids. He also studied the effects on rats of an exclusive diet of horse and of beef muscle (36) and found that not only did young animals die but that the older ones were distinctly inferior in their ability to produce and rear young.

149. **Osborne and Mendel's Studies on the Vitamin Content of Animal Tissues.**—Osborne and Mendel (37) have shown that muscle tissue is very deficient in the anti-neuritic factor, water-soluble B, and in the anti-ophthalmic factor, fat-soluble A and that it contains but very little of the anti-scorbutic factor, water-soluble C. Meat extracts were also deficient in these respects.

In marked contrast to the results with muscle tissues are those obtained with the glandular organs. McCollum and Davis (38) showed that an ether extract of pig kidney or of codfish testicles is a good source of fat-soluble A. They also showed that heart muscle is decidedly deficient in this substance as compared with kidney. These results for heart and kidney were verified by Osborne and Mendel (37). These authors also showed that liver is a good source of fat-soluble A, and water-soluble B. The liver, when fresh, is rich in anti-scorbutic properties (39). Osborne and Mendel have found that the proteins of muscle, liver, kidney and brain are complete as sources of amino acids for the support of growth when each serves as the sole source of protein in the diet.

These findings are in harmony with the studies of Cooper (40), who made a comparative study of the relative values of a series of food-stuffs for the prevention of polyneuritis in birds. The results were expressed in terms of grams of fresh substance per day necessary to prevent the development of the disease. These values are as follows: Ox muscle, 20; ox cardiac muscle, 5; ox cerebrum, 6; ox cerebellum, 12; ox liver, 3; sheep cerebrum, 8-15; fish muscle, more than 10; egg yolk, 3; cow's milk, more than 35; cheese, more than 8.

As a source of protein for the support of growth the kidney is greatly superior to muscle tissue. Liver appears to fall between these in its value as a source of amino acids.

150. **Muscle Meats Differ Greatly in Their Dietary Prop-**

erties from the Glandular Organs.—In meat eating of the type so common in America, in which ham, steaks, roasts, chops, and other cuts which are derived from muscle, are almost exclusively used, the only important supplementing effect of meat on the remainder of the diet lies in the enhancement of the protein and in the increase in the phosphorus content. When glandular organs are eaten, these add considerable amounts of fat-soluble A and water-soluble B, but when cooked, no water-soluble C. In general we eat so little of the glandular organs that this source of the uncharacterized factors is nearly negligible.

The liver and kidney are, however, so exceptionally valuable in enhancing the biological values of certain cereal grains, that they may well find a regular place in the diet under certain conditions where it is desired to have a low protein intake of exceptionally high quality (41).

151. **Animal Fats.**—These have been studied to determine their value as a source of fat-soluble A. This substance, it will be remembered, is especially abundant in butter fat, egg yolk fat and in the leaves of certain plants. McCollum and Davis (42) and also Osborne and Mendel (43) found that lard had no appreciable growth-promoting properties when added to a diet complete except for fat-soluble A. Osborne and Mendel showed that cod liver oil is an excellent source of fat-soluble A. They examined the more liquid portion of beef fat and found that it contained in demonstrable amount the dietary factor in question, whereas the unfractionated fat was very poor in it (44). Halliburton and Drummond (45) obtained similar results in their study of the nutritive properties of various kinds of margarines.

Recently Daniels and Loughlin (46) have presented data which indicate that some samples of lard contain demonstrable amounts of fat-soluble A. For periods of five months they were able to secure growth in young rats with diets containing 28 per cent of lard as a source of this dietary essential. In other experiments where but 21 per cent was used the animals were not able to grow after two months. The findings in our own laboratory indicate that there was probably a certain amount of fat-soluble A in their ration derived from the extract of wheat germ added for the purpose of supplying water-soluble B.

These results are not to be interpreted as indicating that lard is in any sense comparable as a source of this dietary essential to the fats of milk, egg yolk or the leafy vegetables. It is doubtless true that the body fats of all animals which have been fed

liberal amounts of a forage plant will contain sufficient amounts of fat-soluble A to make possible a short positive demonstration of its presence. It should be kept in mind that when questions relating to the adequacy of human dietaries are to be judged from the results of animal experiments, the content of the material fed, and the life history of the animals must be taken into consideration. The dietary history of the animals from which came the fat used in feeding should be considered, in order to make it clear whether the samples examined were typical. It seems that the products used by Daniels and Loughlin were not representative of lards in general.

152. **The Biological and Nutritive Properties of Muscle Tissue.**—The muscle tissue of an animal consists of highly specialized substance the chief function of which is to do mechanical work through contraction. In this process it derives the energy from glucose or from fat. It is, in addition, a storage organ for glycogen, or so-called animal starch, and for fat. It contains but little of cellular structures which are the seat of chemical activity, such as are exhibited by the glandular organs. Chemical analysis shows muscle to consist for the most part, aside from the reserve food-stuffs, of water, protein and salts. The glandular organs yield relatively much nucleic acid while the muscle yields but little. The inorganic content of muscle resembles that of the seeds of plants rather than that of the leaves. Its ash is highly acid, whereas that of leaves is highly alkaline. Muscle is, however, very poor in magnesium as compared with any vegetable food materials, is rich in phosphorus, and contains much more iron. Since it is also very poor in fat-soluble A, it does not supplement the seeds in any appreciable degree except with respect to the protein factor.

It follows, therefore, that we should not expect to secure growth and normal nutrition with mixtures of seeds and muscle meats. Experimental trials have shown that this is the case. Such mixtures require supplementing with respect to calcium, sodium and chlorin, just as do seed mixtures alone. In most instances such mixtures will also require to be supplemented with fat-soluble A before they will constitute diets which are satisfactory for normal growth and for the support of females during gestation and nursing of the young. It is doubtless possible that with yellow maize or millet seed in the diet in very liberal amount, this factor may be of sufficient quality to permit over a considerable period of time of apparently normal functioning.

It seems highly probable, however, that even with diets of this special selection, animals would be benefited by a more liberal intake of fat-soluble A. Meat and seed diets can be supplemented with liberal amounts of the edible leaves, so as to make good their dietary deficiencies to an extent which will bring about approximately normal nutrition provided the right selection of seeds and leaves is made. Our knowledge in this direction is still very fragmentary.

The glandular organs are not superior to the muscle tissues in their mineral content. They are vastly more satisfactory as sources of protein, fat-soluble A, water-soluble B and water-soluble C.

153. **Dietary Habits of Carnivorous Man and Animals.**—The pronounced deficiencies of muscle tissue as a food-stuff naturally suggest the question as to the reason for the success of the nutrition of the strictly carnivorous animals. This explanation is found in the selection these animals make of the parts of their prey. The carnivoræ are all fond of blood, and it is their custom to open the jugular veins of a freshly killed animal and suck blood as long as it will flow. After blood, the glandular organs appeal most strongly to them in temperate and tropical regions, but in the Arctic the second choice, or even the first may be fat, depending on the previous state of nutrition of the animal. If it has recently ingested liberal amounts of protein it may take only fat from the victim serving as its next repast. This is said to happen frequently in the case of polar bears. A seal is often found by explorers, stripped of its fat but otherwise untouched. The demands for energy are so great in these bears as to make it necessary to consume fat frequently and in large amounts. Since the protein metabolism is of much smaller magnitude, meat of either the glandular or muscle type may be taken at much longer intervals.

When the American Indians subsisted on the bison of the great plains, bone marrow was regarded as a morsel of the greatest delicacy, and this is also true to-day of the inhabitants of Arctic America. So far as possible blood is either used fresh or is preserved for making soup. Most of the Asiatic, and some of the European peoples have no abhorrence for blood as a food. In China blood is regularly sold as food, and in Europe blood sausage is a common article of diet.

154. **Certain Strictly Carnivorous Diets Are Successful with Laboratory Animals.**—When we make a mixture of equal

parts of blood and muscle and confine young rats to it they may grow in a fairly normal manner, whereas with either of these two tissues alone they will suffer disaster (47). Mixtures of blood, liver or kidney, muscle and bone may be so selected as to proportions as to make a very satisfactory diet (31). Here, again, the controlled experiment of the laboratory reveals the secret of success in the nutrition of a class of animals whose excellent physical development on a diet derived solely from animal tissues has often been interpreted as signifying that meat, in the general sense in which we use this term, is a complete food and one of exceptional value for promoting vigor. The meat-eating of the peoples of the temperate regions of America is limited essentially to the consumption of muscle tissue. In dietary properties this is the poorest part of the carcass. Those who take a varied diet in which cereals and potatoes form the most prominent sources of energy, are guided by their sense of taste to select muscle meats rather than other meats superior in dietary value.

155. **The Successful Rearing of Young Lions.**—An interesting example of the importance of making a proper choice of animal parts in order to make a complete diet, is afforded by the experience of those who have attempted to rear young lions in captivity. With few exceptions in the past such attempts have proven failures, since the animals developed rickets. If they survived they were so deformed as to be unfit for exhibition purposes. In recent years in at least two zoölogical gardens these animals are now reared successfully. A young lion cannot grow normally on a piece of muscle meat with a large, hard bone attached. In many cases the large bones given them were so hard that little could be gnawed therefrom. When these animals are fed with liver, fat, and bone of a type which they can eat in considerable amount without danger of choking, and when their diet is varied frequently with small animals which can be consumed entirely, such as rabbits or pigeons, they grow up strong and beautiful.

156. **Dietary Properties of Muscle and Those of Glandular Organs Contrast Sharply.**—Too much emphasis cannot be placed upon the dietary deficiencies of muscle meats such as beefsteak, ham, roasts and others of this class. Scarcely anything more detrimental could be done to a young animal than to restrict it for a few weeks to a diet exclusively derived from such meats. It is imperative that we understand the marked differ-

ences between our kind of meat eating, which calls only for meats of the muscle class, and that of the successfully nourished carnivorous animals. The latter eat liberally of several parts of the bodies of their prey which have much more satisfactory dietary properties than the muscle tissues, and thus secure a properly balanced diet. The glandular organs are much better constituted as food, than are the muscles, and these should be selected oftener than they are at present in America. The liver, kidney, sweetbread, etc., are not complete foods in the sense that they furnish the proper amounts of each of the dietary essentials for the nutrition of the body, but they are among those best constituted, and are vastly superior to any other animal tissues. The glandular structures are, like muscle, lacking in calcium, and should always be supplemented with some food rich in this element. This is the only deficiency in this class of foods of animal origin. Meats of all kinds have a very great value for enhancing the values of proteins of the cereal grains.

157. **Milk.**—This is the most satisfactory single article of food which is suitable for consumption by man. It is not an ideal food when taken over a long period as the sole source of nutriment, but is the best one with which nature has provided us. It is the one food for which there is no effective substitute.

Milk is a very effective food for supplementing the deficiencies of other substances such as the cereal grains, tubers and fleshy roots (48). It is rich in both calcium and phosphorus, and many vegetable foods are relatively poor in both these elements, especially the former. In fact, there are but two classes of foods which are relatively rich in calcium, the principal element in lime, and a prominent constituent of the substance of bone. These are the milks of various animals and the leafy vegetables. All other kinds of foods fall below the nutritive requirements of man and animals in this substance. The body is very sensitive to deviations from the optimal concentration of calcium in the food, and serious damage may easily result to the bone structures if the diet is not properly constituted with respect to this substance.

158. **Milk Is Deficient in Iron.**—The most marked deficiency of milk is in its content of iron, which is very low. The newborn mammal is provided with a store of this element in its tissues, sufficient to tide it over the period while it is on an exclusive milk diet, but if a child were confined too long to milk as its sole food it would suffer from anemia for lack of iron.

Milk is a water rich food, containing about 87 per cent of

water and 13 per cent of dissolved substances consisting for the most part of proteins, milk sugar and fats (49). It is too bulky to be satisfactory as the sole food for the adult, because of the difficulty of taking a sufficient amount to cover the energy requirements. It is, therefore, to be valued essentially as a food for supplementing other foods and for specifically correcting their deficiencies. The striking fact brought out by modern nutrition investigations is that most animal and vegetable foods are singly or collectively faulty in sufficient degree to interfere seriously with the physical development of the young and to lead to early deterioration of the adult. The most important consideration to be kept in mind is, therefore, the selection of food so as to compensate the deficiencies of one article by those of another and thus make a properly balanced dietary. For this purpose milk is truly the ideal food. The property of enhancing all the deficiencies of cereal grains, legume seeds, tubers, roots and muscle meats, is possessed only by milk and the leafy vegetables, and for this reason McCollum proposed, in 1918, that in order to make these two classes of foods stand out in importance as they deserve to do, they should be designated "protective foods" (50).

The supplementary value of milk for other foods depends upon its unique calcium content, on the quality of its proteins, especially their special fitness for completing the amino-acid quota and balancing the same, in vegetable foods of the storage tissue class, and on the quality of its fat.

It is of great interest that recent investigations which were sufficiently extensive to make them conclusive, have shown that the proteins of muscle, liver and kidney, are in general more valuable for enhancing the values of cereal and legume seeds than are the proteins of milk. It is only in this respect, however, that the animal tissues surpass milk (51).

159. The Fats of Milk a Good Source of Fat-Soluble A.—The fats of milk are the most important source in the American and European diet of the dietary essential fat-soluble A. This, as has been pointed out, is not abundant in any seeds, tubers or roots, as compared with the amounts of it contained in butter fat of good quality. This is the anti-ophthalmic substance, fat-soluble A. It is essential for growth or for normal maintenance. This substance will be considered more in detail in a later chapter in connection with the deficiency diseases.

160. Milk Is Frequently Soured to Preserve it from Un-

wholesome Decomposition.—Milk is not only the most perfect human food but is likewise an unsurpassed nutrient medium for the growth of bacteria. Hence it is very liable to become unwholesome through the agency of microörganisms unless it is properly handled. In hot countries and among pastoral peoples who live under primitive conditions the practice is to promptly sour all milk by permitting a vigorous growth of certain races of lactic acid-producing bacteria in it. This protects the milk against proteolytic organisms which produce unwholesome decomposition products, because the rise of acidity is so rapid that all forms other than the acid-forming organisms and certain yeasts are killed or their growth inhibited. Sour milk is a highly wholesome food, and is used in enormous quantities in Asia, Arabia, the Balkan States, Northern Africa and in the grazing sections of Abyssinia. Wherever it is used in liberal amounts as human food, the people are of exceptional physical perfection. This will be further discussed later.

The number of bacteria in milk depends upon the temperature and age and the amount of dirt which is allowed to contaminate it. In America it is the custom to market liquid milk either raw or pasteurized. In order that this may be done in a satisfactory manner great care must be exercised in respect to cleanliness of cows and of milkers and of utensils; and refrigeration must be immediate and effective and delivery prompt. There has been steady progress in the supervision of the milk supply of cities in recent years and American cities have the most wholesome milk supplies in the world. All city milk supplies should be pasteurized. This is effected by heating the milk during thirty minutes to a temperature of 145 degrees, followed by prompt cooling and bottling in sterile containers. This prevents the spread of typhoid fever, scarlet fever, tuberculosis and other diseases which are sometimes milk borne.

Bacteria in milk are related to infant mortality. Children fed clean milk with few bacteria have a lower death rate than those who take milk with high bacterial counts. Many organisms which are relatively harmless to adults may cause diarrhea in infants and young children, or at least set up intestinal inflammation.

161. City Milk Supply Should Be Rigidly Inspected.—The desirability of thorough control of a city milk supply through the agency of the health department has been fully justified by the results. Bacterial counts should be made regularly of market

milk, (1) as an indicator of the care exercised in keeping healthy cows and in exercising cleanliness on the farm, refrigeration and promptness of delivery; (2) as a basis of condemning milk which is unwholesome because containing dirt, filth, or decomposed materials. Dairy inspection has come to be a well recognized method of insuring a wholesome milk supply.

162. **Eggs.**—Eggs contain everything that is necessary for the growth and maintenance of the body, but are particularly lacking in calcium, and are unbalanced with respect to certain other food principles. Thus, eggs are very rich in fats and related substances, and are nearly lacking in carbohydrates. A diet exclusively of eggs, or in which eggs are a prominent constituent will favor putrefactive processes in the alimentary tract. For these reasons, eggs are to be regarded as articles which should be of secondary importance so far as amount is concerned. They have, however, most exceptional dietary properties which makes it desirable to use them where the item of expense is not prohibitive.

The fats of eggs are fully comparable with butter fat as a source of the fat-soluble A (42), and egg yolk is at least comparatively rich in water-soluble B, and in water-soluble C. The proteins of egg are believed to be of high biological value. In the developing chick there is considerable absorption of lime from the shell, and in this way the shortage of calcium in the organic content of the egg is made good. When we eat eggs, we cast out the shell and thus take the part which is deficient in lime.

It will be seen, therefore, that eggs may have an important place in enhancing the quality of a cereal, tuber and meat diet, but that they cannot logically be considered a substitute for milk. They should be eaten with a diet rich in carbohydrates to discourage the tendency for putrefaction in the intestine, which they favor, and should be used to confer palatability on other foods rather than as a prominent constituent of the food supply.

163. **Sea Foods.**—Foods of the class to which oysters, crabs and clams belong, assume a new importance in the light of the nutrition studies which have so clearly shown the inferiority of muscle meats as compared with the secretory organs and tissues which are concerned with the transformation of foods to end-products of metabolism, i. e., the glandular organs (52). In clams, oysters and soft crabs, we eat the entire animal except its exo-skeleton, the shell. This insures the consumption of tissues containing all the uncharacterized food substances, and makes

these articles of diet, supplementary foods in the sense that they are likely to add to the diet some principles which it in many instances contains in amounts below the optimum.

While such articles are not necessary in a diet which contains the requisite amount of milk and the leafy vegetables, and must be regarded as somewhat expensive foods to be eaten as an indulgence of the appetite, the shellfish doubtless played a most important rôle in the nutrition of early man. Numerous shell-heaps or "kitchen middens" of enormous proportions occur on the Atlantic coast of America and Europe. These were the sites of human habitations over long periods and indicate that these shore dwellers depended in great measure on shellfish for their sustenance. Their type of diet represented a peculiar kind of carnivorous feeding which was very satisfactory.

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CHAPTER VII

THE VEGETARIAN DIET

164. **Vegetarianism Generally Practised as a Dietary Fad.**—There has always been a tendency for dietetic theorists to advocate the adoption of a fleshless diet. The proponents of this system have broken up into schools, the adherents of which differ in the fervor with which they espouse their cause. The most extreme of these are the enthusiasts of the fruit and nut diet (1), who experience esthetic pleasure in the thought that their foods grow and ripen away from contact with the soil and suggest, therefore, the purity and fragrance of orchard and forest, the poetic joy of summer and the inspiration of the rural landscape. Another group adopts the vegetarian diet because of an abhorrence of the idea of taking animal life for the sake of food. These two classes of vegetarians regard flesh as unwholesome as well as unethical, and defend with a number of arguments the view that meat eating tends to moral debasement and physical degeneration. The third group, the lacto-ovo-vegetarians, who permit the use of milk and eggs along with a diet otherwise vegetarian, is in general less extreme in its ardor for ethical considerations, and adheres to its tenets because of conviction that it makes for physical efficiency in a greater degree than does meat eating.

165. **Food Faddists Frequently Discredit Themselves by Their Philosophy.**—While some of the arguments offered in sober earnestness in support of abstinence from flesh foods are suggestive of mental invalidism, others demand serious consideration and an answer based upon scientific understanding. In the former category we may place the assertion that the anthropoid apes, regarded as cognates of our ancestors, live on fruits, nuts and cereals, and that this fact proves that such a diet is especially suited to the nutrition of man. One may well argue that if a change to meat eating in the era of the cave man has caused or permitted him to develop mentally and physically into what the human race is to-day, this change in dietary habits may have

been indeed a great piece of good fortune. The low development of other omnivorous types of animals weakens the force of this argument. We may also retort that it is no more advisable to permit the apes to be our guides in dietetics than in certain other ways of living. It is, however, well known that the apes eat insects, worms, eggs, small birds and such other animals as they are able to capture, and that they also eat the leaves of certain plants.

There is little comfort for the vegetarian enthusiast in the comparison of the anatomical structure of the alimentary tract of man with that of animals whose diets are of different types. The dentition, the size and shape of the stomach, intestine and cecum of man clearly indicate suitability for a mixed diet. To the esthetic argument the meat eater may reply that he includes sufficient fruits, nuts and cereals in his diet to permit him to be inspired by the beauties of Nature. To the statement that a refined person cannot eat meat until it is cooked, and its flavor changed so as to disguise its origin, the reply may well be made that many fruits and vegetables are not at all appetizing until cooked and so flavored as to increase their palatability. The argument which was at one time considered to be irrefutable and to be of sufficient force to condemn meat eating rested on the content of uric acid forming substances (purins) in flesh foods. Chemical studies have, however, shown that there are very nearly comparable amounts of purins in many vegetable foods, such as lentils, oatmeal, beans, asparagus, and notably in tea and in coffee.

166. **Meat Eating Cannot Be Condemned as Deadening the Moral Faculties.**—A stock argument of radical vegetarians is that meat eating deadens the moral and intellectual faculties. One who reflects that Moses, David, Solomon and Jesus ate flesh foods cannot be deeply impressed by it. Likewise the statement that animals living on a vegetarian diet are strong and tractable, while carnivorous animals are ferocious does not withstand inquiry. The average bull or belligerent billy goat can strike terror into the heart of man with less provocation than is necessary to render dangerous a lion or a wolf. The gentle and happy disposition of the Eskimo on his strictly carnivorous diet stands in marked contrast to the ferocity with which the vegetarian Bengalese deported themselves during the mutiny of 1857.

167. **A More Valid Argument Against Meat Eating.**—The more valid arguments concerning the use of meat as contrasted

with the fleshless dietary regimen, are based upon the view that meat is unwholesome and that it contains waste products, which, because of their poisonous properties, tend to do damage to the body tissues. This view is upheld by experimental results. Professor Irving Fisher of Yale conducted extensive experiments with flesh abstainers and flesh eaters, and found the former possessed of much greater endurance than the latter. The tests involved holding the arms outstretched, knee bending, and exercises of similar nature. The flesh abstainers were three to six times as capable of endurance as were the flesh eaters (2). Similar results have been reported by Kellogg (3).

It would be unprofitable to review further the old debate concerning the relative merits of meat eating and meat abstinence. There was no evidence of a conclusive nature upon which the question could be decided. Those who were not convinced by the results of Fisher's endurance tests and those of others could argue that the vegetarians were enthusiastic exponents of a fad in order to defend which they exerted themselves to the utmost, whereas the meat eaters were not so determined to justify a practice which is all but universal, and which seems to them satisfactory. Hence they did not have the same psychological attitude toward the contest as did their antagonists. There were factors not then appreciated, which are of vital importance in the discussion of the vegetarian diet. These can best be made clear by describing certain experimental work which has a direct bearing on the subject.

168. **Slonaker's Study of the Vegetarian Diet.**—The most elaborate attempt to test the relative merits of the strictly vegetarian diet as contrasted with the omnivorous type was made by Slonaker (4). He fed a group of young rats on a list of 23 vegetable foods, allowing them free choice within limits. For comparison a similar group were fed the same foods of vegetable origin, but in addition animal food was given in moderate quantities. Since several natural foods, raw or prepared, were offered at a time, and the animals were allowed free choice as to what they should eat, and since no effort was made to keep a record of food consumption or of the relative amounts of the different foods eaten, the results cannot be used for critical examination except in a limited way. They are, however, of the utmost interest in showing how far instinct fails to guide an animal in the selection of food. Slonaker's list of foods included nearly everything which a vegetarian in Southern California would be likely

to have on his table and included seeds, the milling products of seeds, leafy vegetables, tubers and fleshy roots.

The vegetarian group grew fairly well for a time, but became stunted when they reached a weight of about 60 per cent of the normal adult size. They never increased in weight beyond this point. The omnivorous controls grew steadily to what may be regarded as the normal size for the adult. The vegetarians lived, on the average for the entire group, 555 days, whereas the omnivora had an average span of life of 1,020 days. The vegetarian rats, in other words, grew to be about half as large and lived half as long as did their fellows receiving animal food. Slonaker drew the conclusion that a strictly vegetarian diet was not suitable for the nourishment of an omnivorous animal, but was not able to give the cause of the deficiency.

169. **Even with Wide Variety Vegetarianism Is Likely to Lead to Disaster.**—The results of Slonaker's experiments were published in 1912, and just at the time when McCollum and Davis were securing the experimental data which revealed the differences in the growth-promoting power of fats from different sources, and which established the existence of a new and hitherto unsuspected dietary essential. They fed rats on relatively pure food-stuffs as described in Chapter II with various fats of both animal and vegetable origin, and found that no fat which was derived from plant tissues could compare in growth-promoting properties with butter fat, egg yolk fats and the fats from the glandular organs. It seemed to them that the most probable explanation of the results of Slonaker was the absence or shortage in his vegetarian diet of the dietary essential furnished so abundantly by these animal fats, and which later came to be designated as fat-soluble A. A low protein intake was possibly another cause for Slonaker's failure. With this idea in mind they tried during the summer of 1914, an experiment similar to that of Slonaker, but so modified as to give the animals a much higher protein intake than his animals probably enjoyed. It seemed that if Slonaker's rats ate liberally of such leaves as cabbage and other leafy vegetables and of tubers and roots the protein content of which in the fresh condition does not as a rule exceed 2 per cent, the protein in the other components of the diet might not have been high enough to give the entire ration consumed a content in their food sufficiently high to promote growth at the optimum rate.

McCollum and Davis, therefore, fed their rats a diet which

afforded a choice among the following list of foods: wheat, maize, rye, oat (rolled), wheat germ, maize gluten, wheat gluten, flax-seed oil meal, green clover, green alfalfa leaves, onions, peanuts, and cooked navy beans and peas. With the exception of the last two articles the foods were fed raw. It will be observed that in this list there are several vegetable foods having unusually high protein contents. Maize gluten, a by-product of starch manufacture, contains about 25 per cent; wheat gluten, prepared by washing ground wheat free from starch, about 85 per cent; flax-seed oil meal, 30 per cent and wheat germ 30-35 per cent. Since animals are known to grow well on many diets containing 15 to 18 per cent. of protein, it seemed that with this variety to select from one possible cause of failure in Slonaker's experiments, too low a protein intake, would be avoided. McCollum and Davis had at that time not discovered that the leaf of the plant is a moderately good source of the dietary essential fat-soluble A, although it was known that the leafy foods enable herbivorous animals to thrive on diets derived entirely from plant sources. It was then assumed that when both the leaves and so many different kinds of seeds and seed products were supplied, there could be little doubt that everything a herbivorous animal requires was present in the foods.

The rats fed this wide variety of vegetable foods, and supplied with liberal amounts of protein, duplicated in all respects the results described by Slonaker. They grew at about half the normal rate for the first few weeks, then became permanently stunted, none ever reaching a size much greater than half that of the average normal adult. The addition of butter fat to the diet of some of these animals failed to benefit them in any noticeable degree. The answer to the question as to why rats did not thrive on such strictly vegetarian food mixtures was not secured from these experiments. It was, however, soon after learned wherein lay the cause of failure.

170. **Rats Can Be Grown Successfully on a Strictly Vegetarian Diet.**—McCollum, Simmonds and Pitz fed a group of young rats on a monotonous diet consisting of maize kernel 50, alfalfa leaf (dry) 30, and cooked (dry) peas, subsequently dried, 20 per cent. The three ingredients were ground together so that whatever was eaten represented the formula for the diet. The diet induced growth at approximately the normal rate, and reproduction and rearing of a considerable number of young. The young grew up to the full adult size and were successful in rear-

ing a considerable number of their offspring (see Chart 7). Without ever tasting, after the weaning period, anything other than this monotonous mixture as their sole source of nutriment this family of rats remained approximately normal in vigor and successfully weaned the young of the fourth generation with no apparent diminution in vitality. At this point the experiment was discontinued (5).

McCollum, Simmonds and Pitz next carried out another series of feeding experiments with rats, the diets of which were derived solely from a mixture of a leaf and a seed ground together so that the two parts of the ration could not be picked out and separately eaten (6). In marked contrast to the failure of animals to grow on any mixture of seeds, it was found that in many cases a mixture of a seed and a leaf formed a diet on which considerable growth could be secured. Even polished rice, which, as has already been described, requires supplementing with respect to four dietary factors, mineral salts, fat-soluble A, water-soluble B and protein, before it becomes complete for the rat, was found to induce fairly good growth when fed with ground alfalfa leaves in the proportion of 60 per cent of seed to 40 per cent of leaf. On this simple and monotonous mixture young rats grew from weaning time to 83 per cent of the normal adult size. One female even produced two litters of young, but allowed them to die within a few days. A mixture of rolled oats 60 per cent and alfalfa leaves 40 per cent ground together makes a much better ration. On this simple mixture young rats have been observed to grow to the full adult size and to reproduce and rear young. One female reared fourteen out of seventeen young born in three litters. Maize and alfalfa leaf or wheat and alfalfa leaf were not so satisfactory for the promotion of growth as is the corresponding mixture containing rolled oats. Mixtures of the alfalfa leaf with the legume seeds, peas and beans gave still poorer results. The peas and beans were always cooked and subsequently dried before feeding.

These experiences made it evident that there is nothing in vegetarianism *per se*, which makes it impossible for an animal of the omnivorous type to be satisfactorily nourished on this kind of diet. It is only necessary to make the proper selection of food-stuffs, and to combine them in the right proportions. In all the experiments described, in which the diet was made up of so simple a mixture as one leaf and one seed, optimum growth, reproduction and rearing of young were in no case secured.

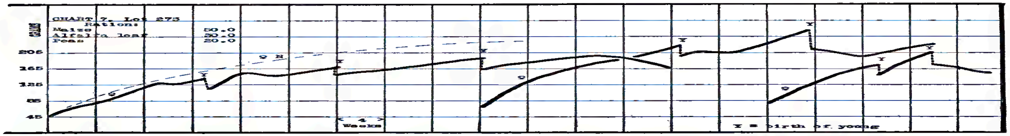

CHART 7.—This series of curves show the records of a mother, her daughter and granddaughter all of which were restricted throughout life to a diet consisting of maize, alfalfa leaves and peas. This simple mixture makes a fairly satisfactory vegetarian diet. This mother and her offspring were not so large as other animals in the same group, but her record is presented because young of the fourth generation, a great-great-granddaughter, was successfully weaned on this diet without any noticeable deterioration in the vigor of the family. The diet was not of the best quality, for the infant mortality was high, and there was a tendency for the animals to remain undersized. It shows, however, that it is easily possible to successfully rear rats on a strictly vegetarian diet.

171. **The Cause of Failure of Slonaker's Vegetarian Rats.** —The failure of Slonaker's rats to thrive on the vegetarian diet is to be explained on the basis of several faults. In the first place, the diet was of such a nature that the animals could hardly do otherwise than take a rather low protein intake. Secondly, the leaves, which formed the only components of the food supply containing enough mineral elements to support growth, were fed in the fresh condition. In this form the water content and bulk are so great that it would be practically impossible for an animal whose digestive apparatus is no more capacious than that of an omnivorous rat to eat a sufficient amount of leaf to correct the inorganic deficiencies of the rest of the mixture, which consisted of grains, seeds, tubers, and root foods. The same physical limitations would likewise determine the failure of the animals to secure enough of the fat-soluble A to supplement the deficiency of all the ingredients of their diet other than the leaves. This would not form so important a fault as the inorganic deficiencies but would be an important depressing factor. Success or failure would also turn in great measure upon the extent to which the animals would be guided by instinct in the selection of the proportions of the several types of food-stuffs offered them. In the opinion of McCollum the appetite is by no means so safe a guide for the proper selection of foods as has generally been supposed.

From the results of the experiments just described it was necessary to conclude that the leaf differs from the seed in the respect that it contains in satisfactory amounts the dietary factors found in the latter in too small amounts. (Compare Charts 7 and 8.) These include the three inorganic elements, calcium, sodium and chlorin, fat-soluble A and proteins which supplement at least in some degree those of the seed. These, it will be remembered, are the three and only purified food factors which need be added to each of the seeds in order to make for dietetic completeness. It is, therefore, possible to devise a diet derived entirely from vegetable materials, which will produce normal growth and optimum physiological well-being.

A point of special interest which it is well to emphasize, is that the bones of these vegetarian rats were of very good quality. There was no evidence in any of the young of the occurrence of rickets, a disease which invariably shows a tendency to develop in young animals restricted to a diet of cereal grains. The exact nature of the defects in the diet which causes this disease of the skeleton cannot be profitably entered into here, but will be con-

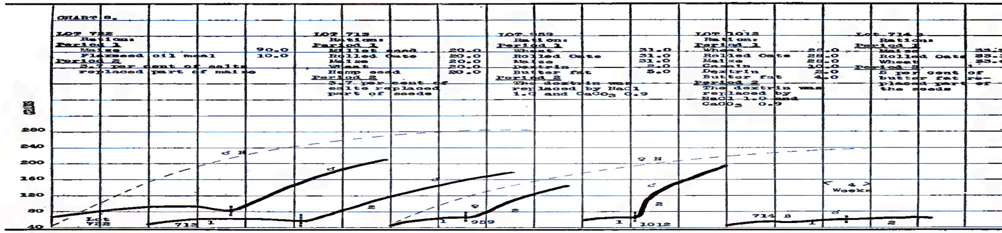

CHART 8.—These curves illustrate the necessity of adding certain mineral salts, especially calcium salts and sodium chlorid, to mixtures of seed products. Lots 722, 713, 959 and 1012 were unable to grow in period 1, but in all cases growth was possible when salt mixtures were added. Lot 714 B made no response with growth when after a period of stunting butter fat was added to their diet. Mineral salts are the first limiting factor in preventing growth in animals fed seed mixtures. Compare with chart 7.

sidered in a separate chapter. It must suffice to say that a satisfactory adjustment among the mineral constituents in the food, and the presence of an organic factor which exerts an important influence on bone formation, are indispensable conditions of normal skeletal development. These conditions are not fulfilled by any diet composed of cereal grains and other seeds. The results of this experiment demonstrate, therefore, that the mineral content of the leaf component of the vegetarian diet employed, supplemented the unsatisfactory inorganic nutrients of the seed portion, so as to favor normal bone development. It is also evident that this diet contained sufficient of the organic factor concerned with the metabolism of the osteoblast, since no skeletal defects were observed. It should also be emphasized that in China and other parts of the Orient where green, leafy vegetables constitute a very important part of the food supply, rickets is almost unknown as a disease of children, whereas it is common in Europe and America, where the tendency in numerous homes is to derive a large part of the food supply from milled cereals, meat, legume seeds and tubers.

172. **Evvard's Studies on the Appetite as a Guide to the Selection of Food.**—At the Iowa Experiment Station, Evvard has conducted extensive experiments of a character which were intended to demonstrate that the appetite and instincts of the hog serve to enable it to make such an adjustment of the relative amounts of the several food-stuffs offered it, as may induce better results in the rate of growth than can be generally secured when the adjustment is made by the feeder, and when the mixture of the ingredients of the ration are offered in a form admitting of no choice by the animal (7). The data secured seem to show that there is some basis for the belief that this element of selection by the animal itself is worth taking advantage of. It should be mentioned that as a rule in all these trials the animals were given a choice of only three foods, one of these being a cereal grain, another, a protein-rich food, and a third a plant leaf. In some experiments a salt mixture was made available. The reasons for the employment of the leaf as a never-failing component of the food supply of the growing pig could not have been explained before the studies of McCollum and his associates with simplified diets and with diets restricted to a single food-stuff. Feeding such diets with single and multiple food additions led to a knowledge of the exact nature of the dietary faults of each. In connection with the types of diets employed by Evvard it

should be mentioned that in case the animal ate fairly liberally of all the food-stuffs offered it, a serious mistake would be hardly made, since the proportions of the several components eaten could be varied to a considerable degree without preventing growth. In the case of the mixture of maize, 50 per cent, alfalfa leaves, 30 per cent, and peas, 20 per cent, described above (Chart 7), it has been found that for the rat these are the best proportions in which these three ingredients can be mixed for the promotion of growth and reproductive processes. It has been further established that with the use of these three food-stuffs a moderate rate of growth may be secured, but that few, if any, young will ever be produced if the mixture fed contains more than 50 per cent or less than 10 per cent of alfalfa leaf. The importance of combining the natural foods in the right proportions is easily seen from these results. It is interesting to note further, that shifting the proportions of maize, peas and leaf in this mixture over a range of 20 per cent does not materially change the protein content, or indeed, the chemical composition of the food mixture to a degree that could be expected to make so great a difference in the state of nutrition of the animals as is actually observed.

There are now available the results of a very extensive series of feeding trials in which the rations were made up of one seed, one leaf and one legume (pea, bean) in various proportions (8). These have failed to reveal any mixture which is quite the equal of the first ration of this type ever employed, that composed of maize 50 per cent, alfalfa leaf 30 per cent, and peas 20 per cent. It is, of course, easily possible that better mixtures of vegetable foods may be found by further effort but these results show very definitely that for the omnivorous type of animal, whose digestive tract is so constituted that the consumption of large volumes of leafy foods *is not possible*, it is by no means a simple matter, to derive the diet entirely from the vegetable foods, and secure the optimum of well-being. The data afforded by the experiments described form a demonstration of the fact that wide variety is of little value as a safeguard to nutrition. Chemical analysis, no matter how accurate and thorough, fails to throw much light upon the dietary value of a food-stuff. The only way in which the problems of nutrition can be solved is through numerous and properly planned feeding experiments. Such studies, however, were not possible before the solution of the problem of successfully feeding mixtures of purified food-

stuffs. These led to the formulation of an adequate working hypothesis regarding what factors operate to make an adequate diet, and made possible the interpretation of the cause of success or of failure with diets of the complexity employed in daily life. It will be shown later that the consumption of milk and its products forms the greatest factor for the protection of mankind in correcting the faults in his diet.

173. **The Deficiencies in Inorganic Elements in Seeds Are Quantitative Rather Than Qualitative.**—The cereal grains contain every inorganic element found in the animal body, and every one which is a necessary component of the diet, but in too small amounts in respect to three to enable the animals to grow. That insufficient mineral matter in a diet may produce grave pathological conditions reveals this moiety in a new and important light. The animal is sensitive either to the actual amounts of certain of the mineral elements in the food mixtures, or to the relationships among them. Sidney Ringer was led in 1891 to his description of Ringer's solution, as the result of the observation that muscle behaves more nearly normally in solutions containing certain salts in definite proportions. Ringer's solution contains for each one hundred molecules of sodium chlorid two molecules of calcium chlorid and between one and two molecules of potassium chlorid, together with a trace of a magnesium salt. Loeb, Howell and others have described many experiments showing the profound effects upon the subsequent development of the eggs, of varying in certain ways the composition of the salt solutions in which unfertilized eggs of certain marine animals were kept (9). In this way the earliest stages of development which are ordinarily observed only in the fertilized egg could be caused to take place in eggs into which no sperm had entered. In the nutrition of the higher animals it had never been made clear how dependent the organism is on the rate at which the blood stream receives mineral nutrients. The fact that the cereal grains are too low in three inorganic elements to admit of growth made it surprisingly clear that food packages just as they come from the hand of Nature are not necessarily so constituted as to promote health.

174. **Vegetarianism Has Been Viewed from the Wrong Angle.**—In the light of what has been presented in this chapter it will be readily appreciated that in the past the vegetarian diet has been discussed from the wrong perspective. It is possible to make a fairly satisfactory diet of foods entirely derived from

vegetable sources, but it is not easy to do so. In general, a vegetable diet will be markedly improved by the inclusion of muscle tissue meats, and more so by the addition of glandular organs, but even these features of the subject are not from the standpoint of good nutrition the most important. It is scarcely practicable for man to eat enough leafy foods to enable him to succeed with the strictly vegetable diet. The limiting factor is the amount of leafy food which can be consumed. Lack of sufficient calcium is one of the most important deficiencies in such a diet, and a great abundance of leaf is necessary to supply this element in adequate amounts.

175. **Some Characteristics of Vegetarian Diets.**—The diet which is strictly vegetarian will practically always be of relatively low protein content. The addition of even small amounts of meat, even of the muscle variety will be very valuable when such a regimen is adhered to. Eggs, because of their relative richness in fat-soluble A and water-soluble B, will be even more effective supplements, and the same statement will apply to the consumption of small amounts of glandular organs. Even small additions of foods of animal origin will tend therefore, to enhance the diet of one who is forced by economic circumstances rather than by ethical considerations, to subsist in the main upon vegetable foods. In another connection we shall present data showing that a diet too low in protein or in which the proteins are of relatively poor quality, exerts very deleterious effects upon experimental animals.

Among the peoples of China and Japan who because of poverty and overcrowding can afford but small additions of fish, poultry or the flesh of mammals to their diet consisting in great measure of vegetable foods, children are schooled from an early age to the consumption of leafy vegetables. Many weeds are eagerly sought after, and trees are stripped of their buds in spring to augment the supply of spinach, cabbage and other leafy foods. An alfalfa field seeded by a missionary (10) in north central China was eagerly appropriated for human food, although it had been intended to serve as a forage for farm animals. Millions of people in Asia have learned the unique nutritive value of green plants, which we in America have never learned to appreciate.

176. **Certain Mineral Elements Are Essential to Normal Functioning of the Tissues.**—So much has been said in these pages of the importance of a suitable content of the mineral ele-

ments which the diet must furnish, that a few words of explanation as to the functions which they exercise in physiological processes may be of value to many readers, who are not physiologists or chemists.

Since the bones consist in great part of calcium, phosphate and magnesium the necessity for an adequate supply of these elements is easy to appreciate. Calcium salts are essential for the coagulation of the blood as it flows from a wound. When this element is removed from a sample of blood it cannot undergo clotting. Certain salts of calcium, especially the chlorid, greatly accelerate the rate of digestion of fats, through the agency of the fat digesting enzymes, or lipases.

For purposes of normal digestion in the stomach the presence of free hydrochloric acid in considerable amounts is indispensable since the pepsin cannot act upon the proteins of the food unless free acid be present. The acid of the stomach is derived from the sodium chlorid or common salt of our food. A liberal supply is necessary, and notwithstanding that the foods all contain a certain amount of it we are impelled by our appetites to make liberal additions of it in cookery, and as we eat, we "salt to taste."

The element sodium, which is a constituent of common salt, is also present in the blood in considerable amounts in the form of the bicarbonate, carbonate and phosphate. These act as "buffer" substances, i. e., they take up and neutralize the acids formed during metabolism, and aid in maintaining the body fluids in a state of neutrality which is a fundamental condition of life.

One of the prominent features of the functioning of living protoplasm is the presence of fluids within it which contain nicely adjusted amounts of certain mineral salts, which maintain what is known as osmotic pressure within the cells and between them and the body fluids.

Potassium is a constituent of all tissues of the body, but the relative amounts in different structures varies considerably. Only when there is a certain relation between the potassium, sodium and calcium concentration in the blood will the heart beat normally. Other functions of the mineral elements could be mentioned, in the performance of which each plays a specific rôle, and in the performance of which one element cannot be replaced by another without causing disturbances of metabolism or even death.

177. **Most Foods Are Too Poor in the Element Calcium.**—

The cereals, tubers and roots must be used in combination with calcium-rich foods such as milk, or leaves, and the addition of meats or eggs cannot take their place. The best type of diet is one which, in addition to moderate amounts of cereals, tubers, legume seeds, root vegetables, and small amounts of meats and eggs, contains liberal quantities of milk, and the leafy vegetables.

Milk supplements any diet to which it is added, in respect to the quality of its proteins, its inorganic content, and its content of the three demonstrated dietary essentials A, B, and C, whose natures are not understood. When it has been heated it lacks the factor C, which is protective against scurvy. Milk is deficient only in iron.

Leafy vegetables possess essentially the same supplementary relations to other foods as does milk. When eaten raw, they are excellent preventives of scurvy, but when cooked they lose most of this property. They are rich in iron.

Eggs have much the same supplementary relations to other foods as has milk, except that they are deficient in calcium, and do not contain carbohydrate, so their tendency is to favor putrefactive decompositions in the intestine rather than to encourage fermentative organisms to develop.

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FIG. 3.—This cow was the same age as that shown in Figure 1. She derived her ration entirely from the wheat plant during the last two-thirds of her growing period. This ration, when submitted to chemical analysis, showed almost exactly the same composition as that fed to the cow in Figure 1. Note the poor nutritive condition of the wheat-fed cow. It has not been possible to prepare a ration solely from wheat products, which will induce good nutrition in animals. Figure 4 shows the typical appearance of the calves produced by cows fed upon a ration properly "balanced," but derived entirely from the wheat plant, and containing the seed, stem and leaf.

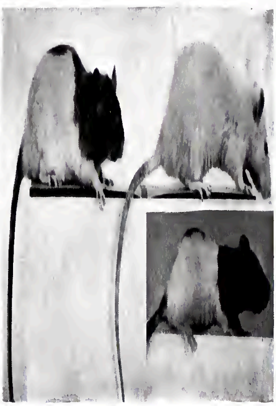

FIG. 8.—This photograph shows the degree of success which has been attained in securing growth, reproduction and rearing of young in an omnivorous animal, the rat, with a diet of strictly vegetable origin. The diet is described on page 161. The data available seem to demonstrate that successful diets of plant origin can be secured only when the leaf of the plant is a prominent constituent of the diet. Those parts of the plant whose functions are those of storage organs (seeds, tubers and roots), do not serve as adequate diets, even when there is a wide variety in the food supply. The leafy structures are so constituted as to correct the deficiencies of mixtures of seeds, tubers and roots.

The albino and her daughter are shown above, and her granddaughter below. Young in the fourth generation were successfully reared, with no apparent diminution in vitality.

CHAPTER VIII

THE DIETARY DEFICIENCY DISEASES

Scurvy

178. **The Relation of the Diet to Certain Diseases Has Long Been Suspected.**—There has long been a belief among both medical and non-medical observers that certain diseased conditions were the result of the continued use of a faulty diet. Of these scurvy has long been the most definitely attributed to unsatisfactory quality in the food. This disease is known to have occurred in the thirteenth century among the armies of the Crusaders during the sieges of Cairo and Damietta. The disease was doubtless almost entirely restricted to soldiers and prisoners until after the discovery of America. This event marked the beginning of long voyages, and scurvy began to take a heavy toll of life among mariners. It became known as "the calamity of sailors" because of its frequency on shipboard. A notable instance in the history of scurvy was the voyage of Jacques Cartier in 1536. While in the St. Lawrence River he lost from scurvy twenty-six of his party, and saved the remainder by the use of a beverage made from an infusion of pine needles (1). The efficacy of fresh fruits and vegetables as remedial agents in the prevention and cure of scurvy was discovered by common experience, and became sufficiently established so that in 1795 the British navy began the regular administration of lime juice to all sailors. This caused the disease to disappear practically in the service. In 1865 the British Board of Trade adopted with equally beneficial results a similar regulation. Scurvy continued to be a menace to all armies until the last few decades, when more effective regulation of the rationing of soldiers has been practiced (2). Until a generation ago the disease was common among miserably fed convicts.

179. **Some of the Symptoms of Scurvy.**—Scurvy develops gradually. The sufferer loses weight, is anemic, pale, weak and short of breath. The gums become swollen, bleed easily, and frequently ulcerate. The teeth loosen and may drop out. Necrotic areas in the jaw bone may result. Hemorrhages into the mucous membranes and the skin are characteristic. In the skin large blue-black spots develop after trivial injury, or even spontaneously. The ankles become edematous, and in severe cases there develops a hard, board-like condition of the skin and subcutaneous tissues. Nervous symptoms of various types are seen, some of which are the result of the rupture of blood-vessels. There follows in the later stages of the disease, headache, convulsions and delirium.

180. **Lime Juice Occasionally Proved Disappointing as an Anti-scorbutic Food.**—Although the experience of the British navy and of several Arctic expeditions had thoroughly convinced physicians and officers of ships that lime juice was a specific remedy for scurvy, there were a number of widely known outbreaks of the disease which kept alive the idea that it was not necessarily due to the lack of some essential substance in the diet. One of these was the experience in 1875-77 of the expedition of Sir George Nares to the polar regions made in the two ships, the *Alert* and the *Discovery*. The crews of both of these suffered severely from scurvy, although lime juice was regularly administered to all the men. It appears that the lime juice carried by this expedition was inferior, and was probably adulterated. The history of this and other early events in the history of the use of anti-scorbutic foods has been interestingly written by Alice Henderson Smith (3).

In 1895-96 the British Army garrisoned at Chitral in India, suffered severely from scurvy, not a man having escaped it, notwithstanding the fact that lime juice was regularly administered daily. In 1902, the men who constituted the party of Captain Scott in his voyage to the Antarctic, developed scurvy in spite of the fact that they were well supplied with West Indian lime juice. On this occasion the men were saved by the substitution of fresh seal meat for canned meats; mustard and cress were grown for consumption in the raw state, and the consumption of bottled fruits was increased as far as possible. It may be said at the outset that the juice of limes grown in the West Indies has been shown to be of but one quarter the value of limes from the Mediterranean region. Doubtless some of the lime

juice provided in those cases where failure of protection against scurvy resulted, was due to adulteration, or to the heating of the juice for the purposes of preservation. It is now known that heating tends to destroy the substance which gives fresh fruits and vegetables their protective value. Recent investigations have also shown that there is a difference in the protective power of fresh and preserved meats. Arctic explorers had great faith in the virtue of fresh meat, whereas experience proved that salted or canned meats repeatedly proved ineffective.

181. **Many Lost Faith in the Efficacy of Lime Juice as an Anti-scorbutic Food.**—The occasions when scurvy outbreaks were observed despite the regular use of lime juice, were widely advertised and aroused in the minds of many the suspicion that scurvy might not be due to lack of freshness in the food. A number of theories were advanced to explain the etiology of the disease. Harley and Jackson (4) in 1900 accepted the view which had been put forth by Torup of Christiania, that scurvy resulted from eating decomposed meat, and was a kind of "ptomain" poisoning. It is easy to understand that this view seemed plausible. The sailors in times when the disease was common were restricted essentially to a diet of salt meat and hard tack. The experiences of men in the Arctic regions with fresh and stale meats confirmed the supposition that the latter were inferior to the former. Stefánsson (5) has recently reported his own observations on this disease in the far North, which led him to conclude that a factor of no small importance was the consumption of large amounts of salt with salted meats, and he therefore resorted as a protective measure to denying salt to his men.

182. **Scurvy Attributed to Acidity of the Diet.**—Sir A. E. Wright (6) compared the symptoms of scurvy with those induced by large doses of mineral acids, and from their similarity drew the deduction that the syndrome was the result of acid intoxication. He suggested that a diet of cereals or of meat or of the two classes of foods used in conjunction produces scurvy because they both contain an excess of mineral elements which in metabolism are converted into acids. He presented data on the chemical composition of a number of food-stuffs which seemed to afford strong evidence that his theory was correct. The following table gives the composition of a list of foods, with their relative yields of acid and base radicals which were worked out by Wright in support of his view. The values represent the oxalic acid equivalent of 100 grams.

Acid Food-stuffs.		*Alkaline Food-stuffs.*	
Oats	1.69 gm.	Carrot	0.61 gm.
Barley	1.19	Turnip	0.32
Beef	0.27	Potato	0.27
Wheat	0.25	Onion	0.25
Egg	0.20	Cow's milk	0.17
Rice	0.10	Ox blood	0.13
Maize	0.07	Peas	0.13
		Lemon juice	0.12
Neutral Food-stuffs.		Orange juice	0.12
Sugar		Beans	0.07
Fats		Sheep blood	0.07

It should perhaps be mentioned that the presence of organic acids in certain of the vegetable foods in the alkaline list, is of no significance in this connection because these are destroyed by oxidation in the tissues.

It will be observed that those foods which were reputed to prevent or cure scurvy all fall in the alkaline group. Wright believed that it was not essential for the diet to contain fresh vegetable foods but that to protect against scurvy it should supply the necessary amount of alkaline radicals to make the diet as a whole somewhat basic. He explained the protection of the Samoyeds of Arctic Russia against scurvy as a result of their consumption of liberal quantities of reindeer blood.

183. **The Classic Experiments of Holst on the Etiology of Scurvy.**—Modern knowledge of the etiology of scurvy dates from the discovery by Holst and Fröelich of the University of Christiania in 1912 (7) that guinea pigs readily develop the disease when confined to a diet of cereals or of bread. These investigators pointed out that the syndrome thus produced was the analogue of scurvy in man, and was characterized by loosening of the teeth, inflammation of the gums, hemorrhages in the joints, decalcification of the epiphyses of the long bones, and the typical histological picture of the bone marrow. They observed that exclusive feeding of guinea pigs with carrots, turnips or dandelion did not lead to this pathological condition, although animals on these foods suffered comparable losses in weight (30-40 per cent). They found that the introduction of small amounts of fresh cabbage or carrots or other fresh vegetables could effect a cure of animals suffering from the disease. They drew the conclusion, which later investigators have abundantly confirmed, that the cause of scurvy lay in the absence of a certain chemical

substance from the "scorbutic" diets. They were able to show that the anti-scorbutic substance is readily destroyed by cooking or drying.

The first to observe the development of scurvy in guinea pigs as the result of restriction to a faulty diet was Theobald Smith (8) of the Rockefeller Institute for Medical Research. In 1895 he described this condition as being induced by limiting these animals to a diet of oats and bran. This chance observation was not followed up by a detailed study, and it remained unnoticed for more than twenty years.

184. **The View That Scurvy Is Due to an Infection.**—The work of Holst and his co-workers did not, however, explain the etiology of scurvy to the satisfaction of all. In 1916 Jackson and Moore (9) made the remarkable observation that guinea pigs fed a diet of oats and milk *ad libitum* develop typical scurvy. Bolle (10) was apparently the first to mention that these animals become scorbutic when fed exclusively on raw or cooked milk. Hart and Lessing (11) had produced scurvy in monkeys by feeding with condensed milk, rice and dried pignuts. Milk is known to be a complete food for young animals, and to induce normal growth for months during the suckling period when it constitutes the sole source of nutriment. This naturally suggested that some factor other than diet entered into the etiology of the disease. Jackson and Moore were able to isolate after death a diplococcus from the tissues of scorbutic guinea pigs. These organisms cultivated in the laboratory and subsequently innoculated into pigs kept on a normal diet capable of maintaining health, produced hemorrhages. The organisms were some weeks later again isolated from the lesions. These findings seemed to afford strong evidence that scurvy may be induced by bacterial infection (12).

184. **McCollum and Pitz Drew Faulty Deductions from Their Experiments on Scurvy.**—The significance of the observation that guinea pigs develop scurvy when fed on oats and milk seemed even more important to McCollum and Pitz (13) than to Jackson and Moore. McCollum and Davis (14) had in 1915, as the result of extensive studies on the nutrition of the rat, formulated the working hypothesis that the simplest diet which can support normal nutrition in this species is one which fulfills the following conditions. It must contain sufficient protein of the "complete" type; adequate amounts of nine mineral elements in appropriate combinations (Na, K, Ca, Mg, Cl, P, S, Fe, I); a

source of the carbohydrate glucose, and two dietary factors of undetermined chemical nature, which McCollum and Kennedy (15) provisionally called fat-soluble A and water-soluble B. These were recognized as belonging to the class of food substances which Funk (16) had designated by the term "vitamine," and for the existance of which he had positive evidence only in the case of the anti-beri-beri substance (water-soluble B) with which polyneuritis in birds and beri-beri in man had been successfully treated. The history of the investigations which led to the discovery of these has been presented in Chapter II.

McCollum had found that a diet of oats and milk sufficed to maintain a rat in a state of health for a long period, without any evidence of disease. When McCollum and Pitz, independently of Jackson and Moore, observed that guinea pigs confined to a diet of oats and milk quickly succumb to scurvy, they found it difficult to believe that the disease could be due to the lack of a specific substance, for milk alone suffices as the sole food for all young mammals during a critical period of their lives. It was difficult to accept the view that anything essential for normal nutrition was absent from milk and oat mixtures.

They further observed that their guinea pigs which were suffering from scurvy developed impaction of the cecum when the condition was brought about by feeding milk and oats, both of which are constipating foods. They, therefore, offered the tentative explanation that injury to the cecum of this species is of primary importance as a factor in the etiology of scurvy. They were inclined to accept the view of Jackson and Moore that the cause of the disease was an invasion of the tissues by bacteria, made possible by the damage to the cecum as a result of the retention of feces. The observation that paraffin oil or cathartics sometimes saved scorbutic animals from death lent support to this view.

185. **The Earlier Views of Hess and Unger on the Cause of Scurvy.**—Immediately after the appearance of the paper of McCollum and Pitz, Hess (17) presented a study of infantile scurvy which seemed to support strongly the view that scurvy is not simply a deficiency disease. He observed that infants fed milk which had been pasteurized at 145 degrees for thirty minutes did not develop scurvy, whereas others fed the same milk but which had been allowed to age for twenty-four hours on ice did so. Milk which had been pasteurized at 165 degrees was found to be more likely to induce scurvy than milk which had

been pasteurized at the lower temperature. Hess also found that aging of raw milk also increased its liability to induce scurvy in infants. The degree of heat to which the milk had been subjected seemed not to be the most important factor, for according to his experience boiled milk did not produce the disease. The most plausible deduction from these observations appeared to be that boiling tended to render the milk sterile, whereas heating to 165 degrees killed for the most part the lactic acid forming bacteria, leaving the more resistant spore-forming organisms in the milk, where they could develop rapidly because with aging the lactic acid content would not rise and hold them in check as is the case in milk which is soured in the normal manner. Milk which was pasteurized at 145 degrees, and milk which was aged, both developed flora which might with reason be supposed to be detrimental to an infant. Hess drew the conclusion that it was the staleness, and therefore the bacteriological condition, rather than the temperature to which the product had been heated, which determined whether or not milk would tend to cause scurvy in the infant.

As the result of later studies, however (18), Hess was led to abandon this theory and to accept the view that scurvy is a deficiency disease, and that it is prevented or cured by the administration of an anti-scorbutic substance.

The appearance of these papers aroused a number of investigators to renew the study of the etiology of scurvy, and the various theories concerning the etiology of the disease soon were subjected to the test of new experiments. Two papers among these deserve special consideration since they completely explained the errors into which several workers had fallen, and fully established the correctness of the view of Holst that scurvy is indeed a deficiency disease of a specific nature.

186. Chick and Hume Confirm the Views of Holst.—In 1917 Chick and Hume, of the Lister Institute, extended the observations of Holst and his co-workers by making a comparative study of the values of a number of food-stuffs as protectives against scurvy (19). There are two methods which may be employed for the study of such a problem. One is to employ animals of a definite and uniform size and add to a scorbutic diet a certain amount of the food under examination to discover whether or not the animals are protected from the disease. The alternative is to produce first the condition and then attempt to relieve the animals by the administration of the food, the anti-scorbutic

properties of which are under investigation. Chick and Hume adopted the preventive type of experiment. They fed their animals oats and bran, which they found would in about three weeks produce scurvy in a guinea pig weighing about 280 grams. The substance to be studied was added in known amount and the duration of the protection, if any, observed.

Chick and Hume emphasized the superiority of this method over the curative type. In the latter the animals return to normal slowly even when the anti-scorbutic potency of the diet is made high, and their improvement is less well marked when it is low. This method leads to confusion in interpretation of results.

As the outcome of their studies Chick and Hume constructed a table (see page 181) in which the protective values of a number of foods are compared. For comparison they likewise included such data as is available to indicate the content of each of the foods in the anti-beri-beri dietary factor (water-soluble B). The latter information was gained by tests of the curative type on pigeons in which polyneuritis was developed by restriction to a diet of polished rice.

In a later paper, Chick, Hume and Skelton (20) discussed their experimental work in relation to the views which had been expressed by the several investigators, who held that scurvy was not a deficiency disease in the same sense as beri-beri or polyneuritis. In the light of their data the erroneous conclusions of McCollum and Pitz were explained. It was shown that the anti-scorbutic value of milk had been greatly over-rated. Chick and her co-workers adopted hand feeding, instead of allowing the guinea pigs to eat of milk *ad libitum*, and showed that when less than 50 c.c. of raw milk daily supplemented a diet of oats and bran it did not defer death from scurvy beyond thirty days or thereabouts. When 50 c.c. of raw milk were actually consumed daily the life of the animals was extended to about seventy-five days. An intake of 100 to 150 c.c. of milk daily served to maintain the animals in a state of health during a period of sixteen weeks, at which time the observations were discontinued.

187. **Milk Not a Very Effective Anti-scorbutic Food.**—It is necessary, therefore, that the diet should consist almost entirely of milk if, through its agency alone, scurvy is to be prevented. Chick, Hume and Skelton point out that this concept is consistent with the rôle played by mammalian milk, which is destined to form a complete food for a definite but limited period in the life of the young.

TABLE XI

VALUE OF FOODSTUFFS AS PREVENTIVES AGAINST SCURVY AND BERI-BERI

– SIGNIFIES NOT INVESTIGATED

Foodstuffs.	*Water Content (Approx.) Per Cent.*	*Value Against Beri-beri.*	*Value Against Scurvy.*
Cereals–			
Whole grain (wheat)	10 to 13	++	0
Endosperm: polished rice; white flour (wheat)	10 to 13	0	0
Bran: e. g., rice; e. g., wheat	10 to 13	++	0
Germ or embryo: e. g., rice; e. g., wheat	10 to 13	+++	0
Pulses–			
Whole (in dry condition)	12	++	0
Germinated pulses (or cereals)	50	++	+++
Vegetables–			
Potatoes	80	0	++
Fresh: e. g., cabbage; e. g., onions; e. g., carrot	90	+	+++
Desiccated vegetables	10 to 15	+	+ to 0 accord. to age
Pickled, e. g., cabbage	–	–	0
Fruit Juices–			
Fresh: e. g., orange; e. g., lemon	90	–	+++
Eggs–			
Fresh	70	++	–
Desiccated	6	++	0
Meat–			
Fresh	70	+	+
Tinned	70	0	0
Milk–			
Cow's (fresh)	87	0	+ (slight)
Yeast–			
Pressed (autolysed)	77	+++	0
Yeast–			
Extract (commercial sample A)	30	+++	0

There is a remarkable difference between the value of certain fresh vegetables as contrasted with milk, for the protection of animals against scurvy. Chick and her co-workers found that 3 c.c. of fresh orange juice or 2.5 to 5 grams of fresh cabbage

leaves when added daily to a diet of oats and bran were sufficient to prevent the development of the symptoms of the disease. These amounts of vegetables were equivalent for the prevention of scurvy, to about 100 c.c. of fresh whole milk which had not been heated.

These studies offer a satisfactory explanation of the observations of McCollum and Pitz who found that guinea pigs which were in the early stages of acute scurvy and at the same time badly constipated as the result of an exclusive diet of oats and milk, could in some cases be cured by the administration of paraffin oil. Harden and Zilva (21) pointed out that any amelioration brought about by the administration of this laxative was due to the increased consumption of milk because of the clearing of the alimentary tract, and consequent improvement in the well-being of the animals.

188. **The Rat and Certain Other Species of Animals Are Immune to Scurvy.**—Mention has already been made of the several factors that must be furnished by the diet in order to render it adequate for the nutrition of the rat (14). It has not been found possible to produce experimental scurvy in this species, and it is necessary, therefore, to conclude that the rat either does not require the anti-scorbutic substance in its metabolic processes, or has the capacity to produce the substance synthetically from some other complexes in the food. If the latter assumption be true the nutrition of this animal would be independent of this factor.

In order to determine which of these explanations holds for the immunity of the rat from scurvy several decisive experiments were carried out in my laboratory in the following way (22): A group of young rats were fed a diet of purified food-stuffs supplemented with an alcoholic extract of wheat germ to furnish the anti-beri-beri factor, water-soluble B. They, therefore, did not have access to the anti-scorbutic factor C, since this is absent or nearly so from wheat germ. To make sure of this fact the extracts were heated so as to destroy any traces which may have been present in the beginning. These rats grew to the full adult size, and remained in good health to the age of fifteen months on a diet which would induce within ten to twenty-five days the severest type of scurvy in young guinea pigs. At this point some of the rats were killed and their fresh livers were fed to young guinea pigs which had been caused to develop scurvy as the result of a faulty diet. In this manner several animals were com-

pletely cured of scurvy by the livers of rats which lacked the anti-scorbutic substance in their diet. There can be but one conclusion from such a result. The rats were able to synthesize the necessary anti-scorbutic substance they were unable to secure from their food. Otherwise it could not have been so abundant in the liver. Man, guinea pig and monkey, however, are all susceptible to scurvy because they lack the synthetic capacity possessed by the rat. Another example of a species which is able to subsist without the anti-scorbutic substance is the prairie dog of the western plains. In my laboratory a young prairie dog born in captivity was restricted soon after weaning, to a diet which would certainly produce severe scurvy in a guinea pig within thirty days. Yet the animal was able to grow in a nearly normal manner and escaped the development of scurvy during a period of ten months. It has not been actually demonstrated that this species, like the rat, has the power to synthesize the missing water-soluble C, for the possibility remains that it does without it without detriment to its health. The idea that its case is analogous to that of the rat seems most plausible.

It has been pointed out that the application of the biological method for the analysis of a food-stuff to the study of the cereal grains has shown that these are deficient in three important respects and are individually or collectively unsatisfactory for the nutrition of the rat. The quality of their proteins is below the optimum; the mineral content is deficient in calcium, phosphorus, sodium, and chlorin, and with the exception of yellow maize and millet seed, they are decidedly low in fat-soluble A. Even when the latter seeds are abundant in the diet the content of fat-soluble A will fall decidedly below the requirement for the maintenance of nutrition over a prolonged interval, or the amount necessary to meet the needs of a female during the period of gestation or nursing.

It was to be expected, therefore, that investigators should, in the light of these studies, appreciate the shortcomings of experiments of the older type in which it was customary to produce experimentally, scurvy in guinea pigs by restricting the diet to cereals. These are deficient from the dietary standpoint as already discussed and in addition are not of a physical texture suitable to the guinea pig. The digestive tract of this animal is fitted only for a diet of succulent foods such as green grass, roots and leafy vegetables. When these are eaten in liberal amounts, grains may form a valuable addition to their diet, but not other-

wise. Any animal which possesses so highly specialized a digestive tract as does the guinea pig, in which the stomach and cecum are very large and delicate, has not been shown to be satisfactorily nourished during long periods on a diet which is thoroughly digested and absorbed, and which leaves little residue, or one which forms hard or pasty feces. The cereal grains leave little residue, and oats and milk form hard and pasty feces.

189. **The Studies of Cohen and Mendel on Scurvy.**—In order to overcome these difficulties Cohen and Mendel (23) prepared a diet of cooked soy bean flour supplemented with 3 per cent each of sodium chlorid and calcium lactate, and dried brewer's yeast, and sufficient raw Jersey milk to furnish 5 per cent of butter fat. The yeast was added for the purpose of procuring a generous amount of the anti-beri-beri substance, water-soluble B, and butter fat for the object of furnishing fat-soluble A.

On this diet, which contained everything necessary for the nutrition of the guinea pig except the anti-scorbutic substance, which Drummond designated water-soluble C (24), young animals gain weight very rapidly, and for a time their appearance is satisfactory. On about the tenth day, however, while still eating well and gaining in weight, they begin to show tenderness of the wrists and ankle joints. Their condition after this time rapidly becomes worse, and the joints swell to two or three times their normal size. The appetite fails and a sharp decline in weight ensues. At this point the animals can be saved by the administration of foods containing a sufficient amount of the anti-scorbutic substance.

Using this diet Cohen and Mendel were able to confirm the observations of Holst and of Chick and her co-workers, and to describe what appears to be simple scurvy unaccompanied by other conditions due to malnutrition. Cohen and Mendel have given the most complete and accurate description of the syndrome of scurvy in the guinea pig. Its onset is usually characterized by tenderness of the wrists, ankles and knees, developing in the order named. Within a day or two the affected joints become swollen, frequently to the extent of two or three times the diameter of the normal bone. Spontaneous fracture of the bones is of frequent occurrence. These conditions are observed especially in guinea pigs which weigh 150 to 250 grams. Older animals lose the use of their hind legs because of stiffening and paralysis. The animals find relief in lying on the side or back so as to favor the affected members. This position has

been described by Delf (25) as the "face-ache" position. If the animals are permitted to remain long on the diet deficient in the anti-scorbutic substance the swellings fail to disappear when the diet is corrected, and develop into exostoses. When curative measures are administered early enough the bones appear to return to normal.

190. **The Anatomical Lesions in Scurvy.**—The two most noticeable conditions observable at autopsy are hemorrhage and fragility of the bones. The stomach, intestines and cecum may show congestion, hemorrhage or ulceration, but according to Cohen and Mendel these organs may in some cases be normal in appearance. These pathological conditions are usually observed in animals fed oats and water or oats and milk, and less frequently in those fed the diet of Cohen and Mendel. These authors point out that an ever present condition in advanced scurvy is lack of appetite for food. They found the food intake to diminish as the disease advances, but that fasting does not produce the characteristic lesions of scurvy. These observations have been confirmed by Lewis and Kerr (26).

A remarkable observation made by Mendel and Cohen is that the swollen joints and tenderness often appear while the animals are still growing rapidly and enjoying a good appetite. Inanition can, therefore, play but a minor rôle, if any, in the production of the more prominent symptoms of scurvy. There seems to be regularly a period of ten days or so of fasting previous to the death of the animals which are confined to the scorbutic diet of soy beans or cereals, for the loss in weight during this period corresponds to the rate noticed in guinea pigs during starvation.

191. **The Anti-scorbutic Values of Some Common Food-Stuffs.**—It remains to record the more significant experimental data which show the distribution of the anti-scorbutic substance, and its tendency to be destroyed by heating, drying or aging, and its synthesis during the germination of seeds.

Chick and Delf (27) studied the anti-scorbutic values of dried peas and lentils and found them to have no demonstrable value. On soaking the seeds for 24 hours in water and germinating for 48 hours at room temperature, the anti-scorbutic value became pronounced. While these sprouted seeds were found to be inferior to orange or lemon juice, or to cabbage or swedes, they were equal in efficiency to green beans or potatoes, and superior to carrots or beet roots. The anti-scorbutic power is greatly reduced by boiling. For this reason they recommend that when

any green food is being depended upon to protect against scurvy it should be cooked as short a time as possible.

Delf (25) showed that a very small amount of raw cabbage is sufficient to protect guinea pigs from the symptoms of scurvy when added daily to a diet of grains and autoclaved milk. Her histological evidence showed, however, that an apparently healthy animal may be in a condition of incipient scurvy as regards the structure of its growing bones.

192. **The Effect of Heat on the Anti-scorbutic Value of Cabbage.**—Delf employed cabbage which had been subjected to various temperatures for different lengths of time, and compared these materials with raw cabbage. The anti-scorbutic factor was found to be very sensitive to temperatures below 100 degrees C. She estimated that 70 per cent of the original value was lost after one hour's heating at 60 degrees, and over 90 per cent after the same treatment at 90 degrees. After 20 minutes heating at 90 or 100 degrees the loss was about 70 per cent or the same as at 60 degrees after one hour. She further pointed out the fact that the rate of destruction of the anti-scorbutic substance in cabbage leaves is increased only about three-fold for an increase in temperature of 30-40 degrees, would be an argument against the view that the heat denaturization of an enzyme-like body is in question. Delf suggests that in cooking green vegetables there will be less loss of anti-scorbutic property through cooking a short time at a higher temperature than at a lower temperature for a longer period. Her experience with cabbage heated at 100° to 130° C. for periods of one to two hours, supplementing the diet of oats and bran, indicates that the destruction of the anti-scorbutic substance, though pronounced, is not so great as the observations of Holst and Fröelich would indicate.

193. **Young Carrots Are Better Than Old as Anti-scorbutic Food.**—Hess and Unger (28) demonstrated the superiority of young over old carrots for the protection of guinea pigs against scurvy. They likewise found that carrots cooked in an open vessel for 45 minutes, no longer afforded protection when 33 grams of old carrots were fed. The same amounts of uncooked carrots were effective. The water in which carrots were cooked had little if any anti-scorbutic properties. Young and fresh carrots withstood dehydration, retaining a part of their curative properties.

194. **Effect of Drying on the Anti-scorbutic Value of Vege-**

tables.—These authors found that a daily allowance of five grams of dried vegetables, added to a diet of oats, hay and water failed to protect guinea pigs against scurvy. They tested a commercial preparation of dried vegetables; carrots dried at room temperature in summer, and carrots dried rapidly at 130° F. a few weeks before the experiment. None of these possessed much anti-scorbutic value. A watery decoction of dried orange peel, on the other hand, was able to protect their animals.

195. **The Effect of Aging on the Anti-scorbutic Value of Orange Juice.**—Hess and Unger (29) found fresh orange juice to be anti-scorbutic, but juice which had been preserved in a refrigerator for three months had lost a considerable amount of its potency. Ten minutes heating at 110° C. did not entirely destroy the value of the juice as a protective against the disease.

These investigators precipitated fresh orange juice with 95 per cent or with absolute alcohol, and found the solution potent, but the residue of no value. Neutralized orange juice given subcutaneously failed to protect animals. They report the successful employment of orange juice given intravenously, after it had been boiled and made slightly alkaline to litmus by the addition of normal sodium hydroxid just before using.

196. **Tomato Withstands Heating Without Complete Destruction of Its Anti-scorbutic Properties.**—Hess and Unger (30) obtained good results with canned tomatoes in the prevention and treatment of experimental scurvy in guinea pigs. They also fed canned tomato to infants, substituting it for orange juice, and found that 15 c.c. per day were well tolerated by infants over three months of age. They recommend this as an economical and efficient anti-scorbutic for children. It appears that the tomato withstands heating with less deterioration of its anti-scorbutic property, than does any other vegetable yet studied. Unfortunately tomatoes are ordinarily little if any cheaper than oranges, and canned tomatoes would not prove economical except in institutions where an entire can could be used at once after opening.

197. **Yeast Has Little or No Anti-scorbutic Value.**—Hess (31) found yeast to be without value for the protection of infants against scurvy, when the autolyzed product was given daily in doses of 15-30 c.c. Wheat germ possesses some anti-scorbutic value, but is not comparable with orange juice. He points out that infants may develop scurvy while gaining steadily in weight. Hess and Unger (32) have described other experiments

which seem to indicate that the alkalization of foods with potassium carbonate tends to destroy their anti-scorbutic value.

198. **Harden and Zilva's Experiments with Lemon Juice Preparations.**—Harden and Zilva (33) made from lemon juice a preparation nearly free from citric acid, which still retained much of its curative power, and was successfully applied therapeutically to infants, guinea pigs and monkeys. These studies strengthen the conclusiveness of the proof that the disease which is produced experimentally in animals is analogous to human scurvy.

199. **Desiccated Fruits and Vegetables Are of Little Value as Anti-scorbutic Foods.**—Much interest has centered upon the question of the merits of desiccated and cooked vegetables as anti-scorbutic foods. Givens and Cohen (34) experimented with cabbage and with potatoes which had been cooked and dried in an air blast at 38-52° C. and at 65-70° C. Their results show that cabbage dried in an air blast at 40-52° C. retains some of its protective properties, and could delay the onset of symptoms of scurvy and prolong life when animals consumed one gram daily as a supplement to a scorbutic diet.

200. **Rate of Destruction of Anti-scorbutic Value of Cabbage During Heating.**—Cabbage heated in an oven for two hours at 75-80° C., then dried at 65-70° C. for several days lost its anti-scorbutic properties. Cabbage cooked for 30 minutes then subjected to drying for two days at 65-70° C., possessed no protective value for animals. Potatoes cooked and dried for two days at 65-70° C. failed, when consumed by guinea pigs to the extent of the equivalent of 5 grams daily, to protect the animals against scurvy.

These results are in harmony with those of Delf and Skelton (35), who made an elaborate study of the value of dried cabbage as an anti-scorbutic agent. They estimated that cabbage dried at a low temperature and stored for two-three weeks, lost more than 95 per cent of its protective value. They concluded that desiccation of vegetables is an economically unprofitable process on account of the deterioration of the specific value of this class of food-stuffs.

201. **The Anti-scorbutic Value of Canned Vegetables and Fruits.**—Campbell and Chick (36) studied the anti-scorbutic value of canned foods. The cans were filled with vegetables, and then to within one-fourth inch of the top with boiling water, and at once hermetically sealed by soldering the lids. Steriliza-

tion was effected by exposure to steam at 100° C. for one and a half hours. The cans were then cooled by plunging them into cold water, and were stored at 60-65° F. By this treatment the anti-scorbutic value of 20 grams of bean pods was reduced to less than that of 5 grams of fresh material. Seventy-five to 90 per cent of the protective power was estimated to have been lost. Under comparable conditions of treatment about 70 per cent of the anti-scorbutic value of cabbage was lost.

202. **Anti-scorbutic Value of Some Indian Dried Foods.**—Chick, Hume and Skelton (36) tested several Indian dried fruits as anti-scorbutics, which have long been esteemed by the native population for this purpose. Their experiments included dry tamarinds, cocum, and mango. The authors concluded that these possessed a definite but small anti-scorbutic value. This was greatly inferior to that of raw cabbage, swedes, germinated pulses, orange juice or lemon juice, in the fresh condition, reckoned weight for weight.

203. **The Anti-scorbutic Value of Some Concentrated Fruit Juices.**—Harden and Robison (37) studied the anti-scorbutic properties of concentrated fruit juices. The volatile constituents of orange juice were found to be valueless. Orange juice was concentrated to a syrup under reduced pressure at 40° C. One gram of this dried juice, equivalent to 9 c.c. of fresh juice, was fed daily during forty days as a supplement to a diet of oats, bran and autoclaved milk. After this the amount was reduced to one-half gram, or the equivalent of 4.5 c.c. of juice daily, and the experiment continued for twenty-eight days longer. The weight of the guinea pig was maintained throughout the experiment, and at autopsy no evidence of scurvy was found. When this desiccated orange juice was preserved during seven months, it was found that there was no demonstrable deterioration as the result of aging.

Concentrated lime juice was prepared by a rapid process in which the heating was continued for less than a minute. The resulting syrup was preserved with twice its weight of sugar. The authors believe that the loss of anti-scorbutic property of this evaporated juice was slight.

Apple juice was evaporated rapidly to one-sixth of its original volume, within one minute. The maximum temperature reached was 102° C. The resulting jelly was found to possess value as an anti-scorbutic food, but the deterioration seemed to be greater than was observed in the case of orange juice. The use of fruit

jellies prepared by this method was recommended where there is reason to suspect a deficiency of anti-scorbutic substance in the diet.

204. **Effect of Ultra-Violet Light on the Anti-scorbutic Substance.**—Zilva (38) studied the effect of ultra-violet light on the anti-scorbutic substance. Lemon juice which had been brought to a H-ion concentration of P_H 2.34, and also some which was made neutral, was exposed to the rays for 8 hours without influencing its properties.

205. **Raw Lean Beef Possesses No Anti-scorbutic Value.**—Dutcher, Pierson and Biester (39) found that raw lean beef does not possess anti-scorbutic properties sufficient to permit of its demonstration by experiments with guinea pigs.

206. **Raw Potato Is a Good Anti-scorbutic Substance.**—Givens and McClugage (40) found that 10 grams of raw potato per day was sufficient to protect a guinea pig from scurvy. A temperature of 35-40° C. for 6 to 8 hours seems to be more destructive of the anti-scorbutic property than 55-60° C. for 4 to 6 hours, and the latter treatment is scarcely as destructive as 75° to 80° C. for 2 to 3 hours. The influence of heat appears to be related not only to temperature reached but to the duration of treatment, the reaction, the enzymes present, and the manner of heating. When potatoes were baked for a short time and then dried, the resulting product possessed protective properties. These observations are in harmony with those of Holst and also of Chick.

It will be seen from the foregoing, that the anti-scorbutic substance is a relatively unstable body, and that cooked foods are in general of little value as a source of it. The tomato appears to be a notable exception. The acidity, or other condition found in the juices of the citrous fruits, serves very effectively to preserve the anti-scorbutic factor in its physiologically active form during heating and drying.

207. **Relation of the Food of the Cow to the Anti-scorbutic Value of the Milk.**—The studies relating to the anti-scorbutic value of milk are of special interest because of their importance in the nutrition of infants. It was shown some years ago by McCollum and Simmonds (41) that neither the anti-beri-beri substance, water-soluble B, nor the anti-ophthalmic substance, fat-soluble A, are present in the milk unless they are supplied by the diet of the lactating animal. If this should be true of the water-soluble C as well, it is obvious that the nature of the

food supply of cows whose milk is to be used for infant feeding, when it serves as the sole source of the protective substance against scurvy, is of great importance. Several investigations have been reported which were directed toward the solution of this problem.

Barnes and Hume (42), Dutcher, Pierson and Biester (43) and Hart, Steenbock and Ellis (44) have studied this problem. The last-named investigators have reported studies of the anti-scorbutic value of milk of cows which had been kept on dry feed for varying periods, as contrasted with that of cows which were feeding upon green pasture. Summer milk was found to be much richer in this respect than winter milk. Fifteen c.c. of summer milk afforded protection against scurvy to a guinea pig during 20 weeks, when superimposed upon a scorbutic diet. For most individuals it was found that as much as 50 c.c. daily were necessary to afford complete protection. Of winter milk from cows which had been fed exclusively on dry feed for many months, 70 c.c. were necessary. Silage or sugar mangels added to a ration of dry feeds did not improve the anti-scorbutic value of the milk in a noticeable degree. Dutcher and his co-workers (45) found 20 c.c. of summer milk superior to 60 c.c. of winter milk in its anti-scorbutic potency. When cows were changed from a ration of fresh green feed, to one of dry grains, hay and fodder, the milk did not fall off rapidly in its anti-scorbutic value, but only after the lapse of some weeks did it become inadequate in this respect. When cows were changed to a green pasture after a long period on a dry feed, their milk very promptly improved in a marked degree in its value as an anti-scorbutic agent.

208. Liberal Amount of Fresh Milk Is Essential for Protection of an Infant Against Scurvy.—Hess and Unger (46) state that an infant requires fully half a pint of unheated milk daily in order to provide it with an adequate amount of the dietary factor water-soluble C. If the milk has been pasteurized, or otherwise heated more will be required to afford protection. Dutcher has recently reported that milk can be heated to the boiling point without the destruction of much of its anti-scorbutic property provided it is kept in an undisturbed condition. If it is stirred or shaken it loses its value in this respect very rapidly. The explanation for this appears to be found in the destructive effects of oxygen on the vitamin (47).

209. **Effect of Drying on the Anti-scorbutic Value of Milk.**—Hess and Unger (48) state that drying does not necessarily destroy entirely the anti-scorbutic value of milk. The temperature and time of drying, and the condition of the milk at the time of drying, are important factors in determining the quality of the final product in respect to its scurvy-preventing value. Hart and his co-workers (49) have presented data which would support the view that milk which has been dried on a drum retains more of its anti-scorbutic value than milks which have been dried by the spray process. The data presented above, showing the results attained by several investigators who have studied the effects of heat treatment on fruits and vegetables, show that the method of study is not sufficiently accurate to warrant confidence that the results can be used safely as a basis of accurate comparisons. Work of this nature, when repeated, is likely to give results more or less at variance with those of former experiments. The only safe attitude toward the use of dried milks in infant feeding is to insist upon the addition of some effective anti-scorbutic food such as orange juice, tomato juice, swede juice, or certain other vegetable juices which agree with infants or young children. It does not seem important to attempt to differentiate between different milk powders as a source of the anti-scorbutic factor.

210. **The Diet of the Nursing Mother Should Contain an Abundance of Anti-scorbutic Foods.**—Cow's milk, and doubtless human milk as well, has relatively low anti-scorbutic value even when derived from a highly satisfactory diet. It suffices to protect the young when the diet is almost wholly derived from milk. When, as is not infrequently done, top milk is employed, modified by dilution and the addition of sugar or cereal water, the infant may be placed in jeopardy with respect to the development of scurvy. In early childhood, the displacement of any appreciable amount of the milk diet by cereal foods is a step of doubtful expediency, and if this course is pursued, fresh fruit juices should never be omitted from the diet under such circumstances.

211. **Relation of the System of Feeding to the Incidence of Scurvy in Infants.**—Further evidence relating to the importance of the mother's diet in the anti-scorbutic value of her milk is afforded by a report made by a committee of the American Pediatric Society in 1898. Among 356 cases of scurvy in infants 10 were infants which had been nursed. The following table

gives very interesting information regarding the anti-scorbutic potency of milks treated in different ways (50).

RELATION BETWEEN THE KIND OF FOOD AND THE INCIDENCE OF SCURVY

Breast milk	12 cases; alone in 10
Raw cow's milk	5 cases; alone in 4
Pasteurized milk	20 cases; alone in 16
Condensed milk	60 cases; alone in 32
Sterilized milk	107 cases; alone in 68
Proprietary infant food	214 cases

The above data point clearly to the easy destruction of the anti-scorbutic potency in milks which have been subjected to manipulation. The occurrence of a small number of cases among nursed infants shows that the meat, bread and potato type of diet which is in such widespread use in this and other countries in recent times, does not suffice for the production by a nursing mother of a milk which is complete for the nutrition of her infant. We have no way of determining how large a number of infants, as a result of taking breast milk of poor quality, have reached the stage of borderline cases of scurvy, but whose conditions had not reached the point where they were clinically recognizable. There is much reason to suspect that it is very large.

The experimental data presented in this chapter, leave no room for doubt that scurvy is a deficiency disease resulting from the lack of a specific chemical substance in the food. This substance is not essential in all mammals, but is indispensable to man, monkey and guinea pig, and apparently also to swine and many other species (51). It has been shown, however, that the rat and perhaps the prairie dog (22) possess the power to synthesize this substance, and are accordingly immune to this "deficiency" disease.

212. **Scurvy Among Infants Is Due to Unnatural Feeding and is Relatively New.**—It is interesting, in the light of the large amount of accumulated knowledge of the etiological factor in scurvy, which the last few years has brought forth, to correlate the history of human scurvy with the changed conditions under which large groups of persons have lived at different times. In very early times the disease attacked chiefly soldiers and prisoners since these were subjected for considerable periods to simple and monotonous diets consisting of dry, cooked or stale foods, chiefly cereal grains and legume seeds. These foods possess high

keeping qualities, and are most attractive to those who purvey for large masses of people, especially when transportation or storage is an important item for consideration.

The sailors did not have scurvy until the days of long voyages following the discovery of America. In these voyages they were isolated from fresh foods for weeks or months. With the advent of steam navigation no special precautions have been found necessary for the protection of sea-faring men against this disease, for they frequently have access to fresh food.

Infantile scurvy is not often mentioned in early medical writings. It was not until about the middle of the nineteenth century that it began to attract the attention of medical observers. The cause of this appears clear. Infants were until the last few decades either nursed or invariably lost. The methods of feeding infants that could not be nursed were so crude and unsatisfactory that success in the rearing of them was rare. Not until the eighteenth century was artificial feeding or mixed feeding mentioned in medical literature. Bread and water, called "water pap"; bread and pulse; small beer with egg, etc., were the common foods administered to an infant which had lost its mother. Usually the unfortunate one died from intestinal infection or inanition before it had time to develop scurvy.

In 1894 Barlow first described a diseased condition which we now know to be a complication of rickets with scurvy in infants, and the syndrome became known by his name. He states that the disease was new in England, but more common in Germany, and that it appeared to be on the increase both in England and America. This paper is the earliest and best description of scurvy in infants, and is one of the classics of medical literature.

213. **Relation of Pasteurization of City Milk Supplies to Incidence of Infantile Scurvy.**—Underwood, in 1793, was the first to use cow's milk as a food for infants in his practice as a midwife (52). About the middle of the nineteenth century the manufacture and sale of proprietary foods began to prosper and with this business, doubtless there was a pronounced increase in infantile scurvy. The development of the science of bacteriology led to the discovery that typhoid fever, bovine tuberculosis, scarlet fever, septic sore throat and other diseases might be borne by milk, and city health officers began a campaign for the pasteurization of the milk supplies of cities. While this practice protected the adult members of the population against the epidemics which had been shown to follow milk

routes, it was a calamity to a large part of the infant life of cities. Milk which was pasteurized was deficient in the anti-scorbutic substance, and the incidence of scurvy among infants tended to increase as the artificial feeding of infants came more and more into vogue. Only through the researches of the last decade, has this danger to infants become fully understood, and the means of correcting this tragic error discovered. In this phase of nutrition investigation, we have another example of animal experimentation contributing a great blessing upon the human race, for without the guinea pig, and systematic experimental studies, years or decades would certainly have passed away before the amount of progress which has been attained even during the past five years could have been achieved. Thenceforward we may confidently look for the protection of babies, soldiers, explorers, and prisoners, as well as the general population, against this distressing malady.

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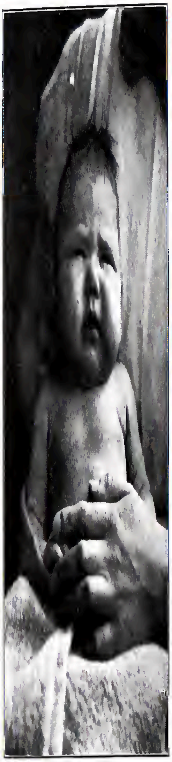

FIG. 10.—Shows edema in a baby fed too largely on skim milk and cereal foods. This condition is frequently associated with incipient ophthalmia of dietary origin.—Courtesy of Dr. Bloch.

FIG. 9.—Illustrates the appearance of a young prairie dog born of animals brought from New Mexico. After weaning time it lived entirely upon a diet which would produce severe scurvy in a guinea pig in fifteen to thirty days and death within a short time thereafter. It grew in what appeared to be a normal manner, and presented the appearance of perfect health, was playful and extremely fond of attention from those in the laboratory. It showed no evidence of developing scurvy while growing rapidly during over six months and during two succeeding months when he did not grow.

CHAPTER IX

THE DIETARY DEFICIENCY DISEASES (Continued)

Beri-beri and Polyneuritis

214. **The Antiquity of Beri-Beri.**—Beri-beri is a disease of great antiquity, which was for a long time confined to Japan, the Dutch East Indies, Malay Peninsula, Philippine Islands, India and Southern China. It was at one time believed to be a tropical disease, but this view has been disproved by its frequent occurrence in recent times in certain other localities, especially in the subarctic regions, notably Newfoundland, Labrador and Norway. It results from faulty nutrition and will occur in any part of the world if man restricts his diet to certain articles of food. In 1914 there was an outbreak of typical beri-beri in the jail at Elizabeth, New Jersey, caused by the poor diet of the inmates (1).

215. **Symptoms of Beri-Beri.**—Beri-beri is a form of peripheral neuritis, the nerves of motion and sensation being chiefly affected. It occurs in two distinct forms, the wet and the dry. Its incipiency is manifested by fatigue and depression, numbness and stiffness of the legs, and more or less edema of the ankles and face. In the dry type, wasting, anesthesia and paralysis are the chief manifestations. The most marked symptom in the wet type is edema, which is sometimes excessive, affecting the trunk, limbs and extremities. In both forms there is generally tenderness of the calf muscles and a tingling or burning sensation in the feet, legs and arms. The mortality in this disease is usually high.

216. **Theories as to the Etiology of Beri-Beri.**—Various theories have been advanced to explain its etiology. Since polished rice is very poor in protein, fat and phosphorus, the prevalence of beri-beri among rice-eating peoples was by some attributed to the low protein content of the diet, by others to fat starvation, to starvation for organic forms of phosphorus, or to intoxication caused by a poison present in rice stored under unfavorable conditions. Climate, arsenical poisoning and specific in-

fection were likewise proposed as factors in the etiology of the disease. It was impossible to determine the true cause of beri-beri until after it had been experimentally produced in animals subsisting on an inadequate diet. It is now generally accepted that the disease is the sequel to specific starvation for a substance of unknown chemical nature, but a very small amount of which is necessary in the diet. This is variously designated as the anti-neuritic substance, anti-beri-beri vitamin, water-soluble B, etc. Beri-beri is, therefore, like scurvy, a dietary deficiency disease, due to lack in the food of a specific substance. The history of the study of this disease by various investigators forms in preventive medicine a chapter of absorbing interest.

217. **The Remarkable Study of Human Beri-Beri by Kanehiro.**—The most notable among the early investigations relating to the etiology of beri-beri is the work of Takagi Kanehiro, Director-General of the Japanese navy. About the year 1880 the disease became a scourge among Japanese sailors. Between 1878 and 1883 the average number of cases treated medically in the navy was 323.5 per 1,000 per year. The incidence of beri-beri during these years average annually 324 per 1,000 men.

During this period the diet of the sailors consisted of polished rice and fish as the principal components, the remainder being derived from a number of vegetables. Takagi, suspected, as the result of a visit to Europe, during which he was impressed with the differences in the diet and in the health of the British sailors as compared with those of Japan, that beri-beri might be due to faulty food. He, therefore, commissioned a training ship to make a nine months' cruise on which the diet of the common sailors included 91 grams of protein per day. The better fed officers did not suffer from the disease, whereas the men were sorely afflicted. There were 169 cases of beri-beri among 276 men during this cruise.

Another ship was then commissioned to make a similar voyage with the protein content of the diet for the common sailors raised to 155 grams per man per day. There was almost no illness during the second voyage, as contrasted with a frightful incidence of beri-beri on the first. Among the crew of 276 men there were but 14 cases of beri-beri. This experience led to a marked improvement of the diets of the personnel of the navy, and the disappearance of beri-beri from the service. The improvement was due to the addition of more meat and vegetables, a reduction of the amount of rice, substituting in part wheat or barley. A

pint and a quarter of milk a day was also furnished each man. This was made possible through the employment of condensed milk. The successful condensation of milk on a commercial scale began in England in 1856. As a result of these changes in the diet, beri-beri became very rare. Diseases of the digestive tract and of the respiratory system became less prevalent and diseases of the eyes were diminished to one half the former incidence (2). The Japanese officials were of the opinion that the increased meat consumption was responsible for the protection against beri-beri.

For many years this experience of the Japanese navy was regarded as a demonstration of the importance of a protein rich diet. That this was not the true explanation of the cause of the immunity of the Japanese sailors to beri-beri, is clear from the history of the disease among the crews of Norwegian vessels. In the invigorating climate of the northern seas, beri-beri suddenly became common among the Norwegian sailors after 1894, whereas before that time it had been quite unknown. Before 1894 the diet of these men consisted of bread made from rye flour, milled without the removal of the germ, peas and salted meat mostly fat pork. After that year it consisted of white bread made from bolted wheat flour, peas, salt pork once or twice a week, preserved meat and fish three or four times a week, and dry fish once a week. Here was a case in which the addition of meat and fish in liberal amounts, although increasing greatly the protein consumption, was nevertheless followed by the sudden appearance of beri-beri, a new disease in that part of the world. It is reported that one sea captain refused to accept the white bread, and provided for his own table a supply of the customary rye flour bread. When beri-beri attacked his crew he was able for a time to afford his men relief by sharing his brown bread with them, but because of the limited supply was forced, finally, to deny it to them to save himself (3). These observations show clearly that meat and bread in abundance, together with some peas, does not constitute a satisfactory diet. When bread is made of bolted flour, and is used as the main article of the diet, the deficiency of the latter in water-soluble B will be sufficiently pronounced to cause beri-beri. Muscle meats and fish also contain very little of this protective substance.

218. **The Classic Experiment of Eijkman on the Production of Beri-Beri in Birds by Diet.**—The most remarkable observation in the history of beri-beri, and the one which inaugurated

the modern era of investigations in the field of nutrition was made in 1897 by the Dutch physician, Eijkman (4). This investigator was medical officer to a prison in Java, where beri-beri was common. He noticed that the poultry which fed upon the garbage of the hospital showed symptoms of paralysis strikingly suggestive of those of his patients, and died with extensive degeneration of the peripheral nerves. Eijkman was led by this chance observation to conduct systematic experiments with chickens and pigeons. He fed some on rice in the natural condition with the husk attached to the grain; others he fed on rice from which the husk had been removed but which still retained the outer layer or "silverskin," and the embryo or germ; still others he fed on rice which had been milled and polished.

The milling of rice removes the bran or cellulose membrane, together with the aleurone layer and the germ. The coating on our polished rice is talcum powder. Eijkman's results demonstrated definitely that rice which had lost its "silverskin" would produce the condition of nerve degeneration to which he gave the name *polyneuritis gallinarum*, and which he rightly considered to be the analogue of beri-beri in man.

Eijkman did not correctly interpret the cause of the production of beri-beri by polished rice and its prevention by the unpolished grain. It has been shown by others that the substance which protects against beri-beri, and which is absent from polished rice, is in great measure concentrated in the germ of the seed. This portion is situated in an exposed position at the tip of the kernel, and is easily rubbed off in milling. On the grain of polished rice, there is a tiny pit in which the germ rested before its removal.

Eijkman's interpretation of the experiments was that the "silverskin" of the rice kernel contained some substance which neutralized the injurious influence of the starch-rich diet. To quote: "Aus den diesbezüglichen Versuchen zog ich den Schluss, dass in den Silberhautchen wahrscheinlich ein Stoff oder Stoffe vorhanden sind, wodurch der schadigende Einfluss der starkehaltigen Nährung neutralisert wird" (4).

219. Climate Not a Factor in the Production of Beri-Beri.—He also studied the influence of climate as a factor in the etiology of the disease, but found it a negligible factor. In the large cities of the East Indies (Batavia, Soeralaja), 66.7 per cent of the people suffered from beri-beri, as against 30.9 per cent among mountain dwellers. The greater number of the first group

ate milled rice. Prisoners fed principally on milled rice showed an incidence of 80 per cent near the sea, as compared with 62 per cent in the mountains. In one prison 5.8 per cent of the inmates suffered from beri-beri when supplied with polished rice, but the disease disappeared when unmilled rice was substituted (5).

220. Other Foods Than Rice May Induce Beri-Beri.—Eijkman tested the hypothesis that a high starch content in the diet predisposed to the disease. He produced polyneuritis in birds by restricting their diets to various Indian starches (Ambon-sago, pearl-tapioca, sago, etc.), and found that the typical symptoms were produced. These experiments were confirmed and extended by Grijns (6), Schaumann (7), and Holst (3). They showed that in addition to polished rice, milled barley, milled wheat, and bread made from bolted flour, tapioca, etc., produced the disease in birds.

221. Schaumann's Studies on the Etiology of Beri-Beri.—Schaumann further demonstrated that dried codfish and pickled meats, heated for a time in an autoclave at 120° C. would produce polyneuritis when the energy requirements of his animals were covered by these foods. He was the first to employ mammals in studies relating to polyneuritis. Dogs, cats, rats, a goat and an ape were used in his experiments (8). He produced the characteristic symptoms of the disease in all these animals, but not in mice. The latter, however, suffered loss of weight and presented signs of malnutrition.

222. The Germ of the Rice Kernel Is Richest in the Anti-Beri-Beri Substance.—In none of these early experiments was the importance of the germ or embryo of the seeds recognized as of special importance. The cortical layer was regarded as the part producing the favorable results. McCollum and Davis (9) in their study of the wheat kernel were the first to call attention to the fact that the germ is exceedingly rich in the substance which is curative for polyneuritis. They suggested that it is the loss of the germ of the rice kernel rather than the cortical layer which robs the seed of its protective power against beri-beri.

These experiments of Eijkman, Grijns, Holst and Schaumann established the fact that the feeding of milled products of the cereals caused the degeneration of the peripheral nerves characteristic of beri-beri. *They did not make clear the cause of this degeneration.* It has been mentioned that Eijkman believed that there was a detoxicating effect of the "silverskin" for the

injurious effects of the endosperm of the rice or other cereal. Schaumann (10) examined the hypothesis that food-stuffs causing beri-beri contain a toxic substance or substances which produce the disease. He was unable to detect any poison which might have been produced as a metabolic product by a microbe. He tested polished rice for acetone, aceto-acetic acid, oxalic acid and oxybutyric acid with negative results. He found the urine of patients did not contain a toxin, and offered the explanation that beri-beri was due to starvation for certain organic phosphorus compounds which were removed during the milling process.

223. **Other Views Relating to the Cause of Beri-Beri.**—In 1899 Laurent (11) attributed beri-beri to lack of sufficient fat in the diet. He believed this type of specific starvation caused a lowering of the vitality and made the subjects susceptible to an infection which was the specific cause of the disease. He attributed the beneficial effects of the addition of meat to the diet of the Japanese sailors, to the increase in the fat content in the food.

Montgomery Smith (12) supported the infection hypothesis. He cited the ship *Lodestar* as having a bad reputation for beri-beri outbreaks. A Japanese revenue cruiser had new cases of beri-beri during successive years while the southwest monsoon blew.

224. **Sir Patrick Manson's Conclusions Regarding the Cause of Beri-Beri.**—Manson (13) deduced from all the evidence which he had accumulated, the theory that the disease was due to a toxin elaborated by a germ growing outside the body. He suggested that improper handling of rice led to its infection and the development of the toxin. He was opposed to the theory that meat in the diet was a protection against the disease, and cited the experience of the Singapore jail, where in 1898-99, there was an ordinary and a penal diet. The former was a liberal one of wheat flour and fresh meat. The penal diet contained no meat. The greater number of cases of beri-beri occurred among those inmates of the prison having meat in their diet. McLeod (cited by Manson) mentions a case where beri-beri attacked the officers on shipboard, but not the common sailors. The former had such luxuries as haddies, clams, oysters, lobster and salmon. It was argued that lack of protein could not be the cause of the outbreak.

Manson also cited the observation of Hirota, who witnessed

52 instances of the development of the disease in nursing infants whose mothers were suffering from beri-beri. When these infants were weaned and fed condensed or fresh milk they recovered promptly, whereas five not so treated died. It was argued by Manson that a child acquiring a germ disease from the mother will not recover so rapidly, but that one intoxicated by taking poisonous milk would be expected to do so. This was interpreted by Manson as supporting his theory of intoxication.

225. **Arsenic Suggested as the Agent Producing Beri-Beri.**—Mention should also be made of the view of Sir Ronald Ross, who believed that beri-beri was due to arsenical poisoning (14). Symptoms of peripheral neuritis have been observed in persons who drank beer containing arsenic.

The view that beri-beri was due to lack of sufficient phosphorus in the diet was supported by Edie and Simpson (15). Polished rice and cereal foods prepared from the endosperm of the grains contain very little phosphorus, and suggested the phosphorus starvation theory. In the light of later experimental studies, these seemingly irreconcilable observations have been made clear.

226. **Fletcher's Studies on Human Beri-Beri.**—The researches of Eijkman, of Schaumann, and of Grijns led Fletcher (16), a physician in the Kuala Lumpur Lunatic Asylum in the Federated Malay States, to carry out a thorough experiment on human subjects, with the object of determining the relation of rice to beri-beri. Fletcher divided the hospital into two sections, each containing nearly equal numbers of patients. To one group he supplied milled rice, and to the other "cured" rice. "Cured" rice was prepared by soaking unhusked kernels, or paddy, for 12-24 hours in water, then heating the soaked grains over a slow fire until they burst. The rice was then spread to dry in the sun. Such rice is easily husked and is ground for use without polishing. The entire kernel, including the germ, was therefore supplied to half the patients. The diet of all the inmates of the asylum consisted of four ounces of fresh meat four times a week; five and one-third ounces of fresh fish twice a week; five and one-third ounces of salt fish once a week; eight ounces of vegetables daily; one and one-third ounces of curry stuffs daily; two-thirds ounce of cocoanut oil daily, and thirty-eight ounces of uncooked rice daily. Since rice absorbs about three times its weight of water on cooking, and becomes very bulky, it seems incredible that so large an amount of rice could be eaten by man.

The only difference in the diets of the two groups of patients was in the character of the rice.

The diets were continued unchanged throughout a year with the following results: The group eating the milled rice developed a large number of cases of beri-beri, whereas no cases developed in the group fed the steamed rice which contained all parts of the kernel. Fletcher rearranged the patients and mingled some of the beri-beri patients with the well, and continued the experiment. The result was a complete demonstration that the disease was due to the consumption of a diet consisting in great measure of meat, fish and milled rice. We now know that the same result will follow the too free use of the endosperm of any of the cereal grains as food.

It has been found by experiments on man and animal, that the germ of rice is especially rich in the protective substance, water-soluble B, a lack of which leads to the development of beri-beri. The diet of the asylum patients observed by Fletcher contained a sufficient amount of this substance when the entire grain was its chief component, but not when the milled rice was used. The diet of the institution cannot be regarded as satisfactory for the promotion of health over a long period of time even when the steamed rice was employed, but it was then sufficiently good to prevent the development of beri-beri. The eight ounces of vegetables, the nature of which were not specified, sufficed to furnish enough anti-scorbutic substance to prevent scurvy. This diet, principally derived from rice, meat, and fish would not, if we may judge from the vast amount of experimental data obtained with animals, maintain over a period of several years normal health in an adult.

227. **Many Grades of Injury Less Severe Than the Clinically Recognizable Deficiency Diseases.**—The tendency of those who have investigated the relation of the diet to disease, as in the experiments under discussion, has been to tacitly assume that a diet which does not lead to clinically recognizable symptoms of malnutrition is essentially an adequate one. The tendency during recent years, while knowledge of the properties of foods and the physiological effects of faulty diets has been rapidly accumulating, has been to appreciate the existence of many grades of malnutrition. It is becoming more and more evident that even slight departure from the optimal in the composition of the food, may lead to states of nutritional instability which become contributing factors to physical breakdown when

hygienic factors are unfavorable, or when infectious processes are operating. Even under the most favorable living conditions, however, there can be little doubt that under such circumstances the body tissues lose their vitality and the span of life tends to shorten.

228. Further Investigations by Schaumann.—After Eijkman's discovery that polyneuritis could be induced in birds on a subsistence of milled rice, Schaumann, in the next few years, showed that pressed yeast, wheat bran and dried testicle of the bull, were all capable when added to such a diet of protecting animals against the disease. Other observers added beans, egg yolk, beef heart, etc., to the list of foods protective against beri-beri. Eijkman used a water or hydrochloric acid extract of rice polish, and found it effective. Schaumann supplemented milled rice with purified protein and with mineral salts, but found that these additions did not prevent the development of the disease. These observations, together with the failure of inorganic phosphates to protect against beri-beri, confirmed his belief that there was a protective substance in certain foods to which he gave the name "activator." He began to correlate the high content of organic forms of phosphorus in rice polish with its curative power. The disease was, he believed, a specific starvation for this "activator," which he believed to be an organic compound of phosphorus. This view was recognized by the Far Eastern Association of Tropical Medicine. They adopted a resolution that rice containing less than 0.4 per cent of phosphorus should be excluded by law from those countries in which this cereal formed the principal food grain. The view that a lack of certain phosphorus-containing substances constituted the etiological factor in beri-beri was, however, soon to be abandoned.

It is easy now as we look back upon the efforts of various investigators to account for the etiology of beri-beri, to understand how so many different views as to its cause could arise. The observations were in themselves generally reliable but it was not possible to interpret them because nobody understood what factors were necessary for an adequate diet, and the specific rôle they played. The existence of certain food substances which are needed in but small amounts, and which serve some purpose other than that of a source of protein or energy, while hinted at by the prevailing views on scurvy, and by one or two students of beri-beri were on the whole practically unappreciated. The recorded speculation regarding them partook of a very hazy and

nebulous character. The experimental demonstration of the existence of such factors by crucial experiments on animals was a matter of great difficulty as has already been pointed out in the second chapter. The history of beri-beri serves as an excellent example of the inability of the student of pathology or of epidemiology to solve the problem of the etiology of such a disease. It illustrates the value of fundamental chemical research directed toward the solution of the problem of the chemical complexes which can serve as the simplest adequate diet for the normal nutrition of man or animal.

Eijkman's experimental production of polyneuritis in birds, which is now generally accepted as the analogue of beri-beri in man, failed to receive for a decade, the attention which it deserved. Finally, however, the significance of his studies became appreciated and a new era in the development of preventive medicine dates from the publication of his paper in 1897 (4).

229. Schaumann's Designation of the Anti-Beri-Beri Substance as "Activator."—It has been pointed out that Schaumann in 1908, sought to explain the etiology of beri-beri on the basis of specific starvation for some organic phosphorus compound. Further studies led him in 1912 to the isolation from rice polishings of a phosphorus-free base which was capable of curing experimental polyneuritis. This substance he called "activator," and assumed that its action was of an enzymic nature.

230. Funk's Designation of the Anti-Beri-Beri Substance as "Vitamine."—Funk in 1912 (17) showed that a substance which was organic and of a basic nature could be isolated from rice bran by extraction with alcohol containing hydrochloric acid, which was precipitable by phosphotungstic acid, silver nitrate and barium hydroxid, and partially by mercuric chlorid. This caused the cure of polyneuritis induced in birds by feeding them polished rice. The following year he confirmed this observation and named the substance "vitamine" (18). In the same year Chamberlain and Vedder (20), and Edie, Evans, Moore, Simpson and Webster (21) confirmed these observations.

231. Suzuki's Designation of the Anti-Beri-Beri Substance as "Oryzanin."—Almost simultaneously, Suzuki, Shimamura and Odaki (19) reported studies almost identical with those of Funk, and fully confirming the latter. They designated the substance which they isolated from rice bran, oryzanin. It thus became established that beri-beri, which is called polyneuritis when it is produced experimentally in animals, is due to starvation for a specific substance, of which but a surprisingly small amount is

necessary to prevent the nervous symptoms characteristic of the disease.

232. **Kohlbrügge's Conclusions Regarding the Cause of Beri-Beri.**—Since the earlier experiments of Schaumann, there had been a tendency to associate beri-beri with scurvy and Barlow's disease. Kohlbrügge (22) associated the occurrence of these diseases with an unbalanced diet too rich in starch. He believed such a diet favored the growth of fermentative bacteria which formed sufficient acids to tend to self sterilization of the intestine, depressing or extinguishing the normal flora. He, therefore, designated them "fermentation diseases." These organisms were believed to occur in rice and other cereals, and were regarded as perhaps related to acetic acid formers. It was postulated that a diet containing free acids tended to hold the injurious kinds in abeyance. This view was opposed to that of Wright (23), who had in 1895 expressed the belief that scurvy was caused by the exclusive use of foods possessing a preponderance of acid elements over bases.

233. **The Year 1912 Saw Great Developments in Our Understanding of the Deficiency Diseases.**—It was in 1912, that the true relation of the diet to scurvy was brought to light. Holst and Fröelich (24) in that year discovered that a diet of cereals of different kinds or of bread caused the development of scurvy in guinea pigs, whereas a diet consisting of cabbage, carrots and dandelion did not cause the disease, although the animals lost 30 to 40 per cent in weight. The latter foods were found to be effective when administered to animals suffering from scurvy, in promptly relieving their symptoms. This, they found, could be done only with raw foods. Either cooked or dried cabbage, for example, was without virtue as an anti-scorbutic food. It seemed that in the course of cooking or drying something essential was destroyed.

234. **The Discovery of Vitamins Did Not Result in an Understanding of Diet.**—Even after these discoveries had been made, however, no one was able to define in chemical terms what constituted an adequate diet. It was beginning to be appreciated that certain substances—vitamin—anti-scorbutic substance—must be taken into account in the planning of the diet in addition to the long recognized dietary essentials. Yet one, and probably two organic factors which are indispensable to normal nutrition in man, remained to be discovered, and future experimental studies were to reveal how surprisingly sensitive is the animal body to nice adjustments among certain of the

inorganic elements. There still remained to learn how widely the proteins of various foods differed in their nutritive values, and there still remained to discover the exact dietary properties of each of the more important natural food-stuffs, which should make it possible to combine them in a manner suited to form a diet of optimal character.

235. **There Are Two Forms of Beri-Beri.**—It has been mentioned that beri-beri occurs in two forms, the wet and the dry. Those suffering from the dry type are usually at least somewhat emaciated, whereas those suffering from wet beri-beri are in a dropsical condition. Until very recently there was no clue to the cause of this difference. A brief history of the observations leading to its explanation will be of interest.

236. **Epidemic Dropsy, War Edema and Wet Beri-Beri.**—There are recorded many instances of the occurrence of epidemics of dropsy during times of food shortage owing to famine conditions brought on by drought, flood devastation or war. In 1876-77 there occurred a famine in India, and in eight famine districts nine-tenths of all deaths were due to famine dropsy, dysentery, diarrhea and debility (25). The Government attempted to operate a system of rationing the sufferers by determining their calorific needs calculated on the basis of body weight. This system proved a failure because those who appealed for relief were found to be either emaciated or apparently very fat. These latter appeared to be in no immediate danger of starvation, and yet they were in many cases in immediate danger of death, because they were not really fat but dropsical. This contrast between one group of the population which was nothing but skin and bones, and another which was bloated as a result of dropsy, occurred in persons of all ages.

In 1899 Patterson (26) described cases of edema among Chinese starving during a period of famine. Weed seeds and greens obtained from wild plants were the only food, and Patterson, who apparently was not familiar with any literature on the subject, called it "greens dropsy." In 1917 the City of Mexico was under military rule for several months and many cases of dropsy developed in persons of all ages. These people had been reduced to beets and spinach as almost their sole food supply.

An epidemic of edema among infants has been reported from Germany by Wagner. It was caused by feeding modified milk alone or modified milk with cereal (27). Potter (28) described an epidemic of dropsy among infants restricted for a time to

barley water, which was very low in protein, inorganic and fat content. Czerny and Keller have called attention to a condition which they speak of as "Mehlnährschaden" literally, a state of malnutrition resulting from too much cereal in the diet (29). This they regarded as the equivalent of saying that they had a diet too rich in carbohydrate, too low in protein and too low in fat. There are, we now know, serious mineral deficiencies, lack of fat-soluble A, water-soluble B and water-soluble C in all cereal preparations, especially when these represent essentially the endosperm of the seed.

Nutritional edema has been many times reported in medical literature. It occurred especially during time of war and scarcity of food. During the great war the condition became known as war edema. In earlier literature it was called by various names such as prison dropsy, hunger swelling, epidemic dropsy, deficiency edema, etc.

Holst (30) states that many cases of dropsy occurred during the Crimean war when there was an epidemic of scurvy. He states that dropsy occurs every year on French fishing vessels off the coast of Newfoundland. Edema was very common among prisoners in England and America during the first half of the nineteenth century. This happened before prisoners received the humane treatment and moderately satisfactory diet now generally accorded them. It was recognized, as some of the names indicate, that it had its origin in faulty nutrition.

Budzynski and Chelchowski (31) described one hundred and ten cases of "hunger swelling" during the war in Poland. These cases resulted from lack of food. It was pointed out that the most marked characteristic of the condition was an edema which resembled wet beri-beri.

Edema has been, as the cases mentioned illustrate, frequently associated with other deficiency diseases, especially beri-beri and scurvy. The histories of the cases recorded, point to a low protein dietary as the condition favoring the development of the disease. Indeed, there is convincing experimental data that seems to prove that protein starvation is the essential specific cause of the condition, but it appears that a water-rich diet poor in protein, especially promotes the development of edema. Maver refers to the occurrence of edema in horses and oxen which work about sugar factories, and subsist for a time upon cane. Cattle fed distiller's wash, or too liberally on beet pulp become dropsical (32).

237. **Experimental Production of Edema Through Protein**

Starvation.—Denton and Kohman (33) have conducted experiments with rats which seem to establish the fact that foods poor in protein and rich in water, tend to cause edema. They restricted young rats to a diet of carrots and found that a large percentage of them suffered from edema. Kohman (34) extended these experiments by feeding carrots supplemented in several ways with purified food substances, and found that edema could be produced only in the animals confined to an inadequate protein intake and given somewhat excessive amounts of water with their food. These results correspond so closely with human experience and with the conditions under which a dropsical state occurs in domestic animals that they seem to establish the cause of edema in times of war and famine.

238. **Sequence of Events as Famine Conditions Approach.**—On the approach of famine conditions due to drought a shortage of forage plants ensues, and the animals, for want of pasturage are killed for food or become too emaciated to be of value for this purpose, and finally die. Green plants fail utterly, and the population becomes restricted to a diet of cereals and other seeds. Since these are the least perishable of our common food-stuffs, they form the last reserve. Especially when rice forms the principal cereal in the diet, the protein content is very low. This is the grain most used in those countries where periodic famines occur, as in India and China.

When famine conditions are brought about by war, circumstances may be very different. The cereals and other seed grains used as human food are at a premium as breadstuffs and meats become scarce and dear, since a large part of the population are called from agriculture to the army or to war industries. The less fortunate of the civilian population come to subsist more and more upon such low protein foods as potatoes and succulent vegetables, together with a limited amount of cereal and little or no meat or milk. It is under these conditions that nutritional dropsy has appeared on many occasions.

239. **Relation Between Wet and Dry Beri-Beri.**—It will thus be seen that there is convincing evidence that in wet beri-beri, protein starvation is superimposed upon a deficiency of the anti-neuritic substance, water-soluble B. Wet beri-beri is a condition resulting from a double deficiency, whereas uncomplicated dry beri-beri would appear to be due to a single deficiency. This is, doubtless rarely the case, however, since the diet is so poor in quality with respect to several factors, wherever beri-beri

occurs, that it can scarcely be regarded as a specific syndrome of an uncomplicated nature. It is this fact that explains the tendency of students of the diseases of dietary origin to emphasize the points of similarity of the two "deficiency" diseases, scurvy and beri-beri. Dilatation of the right side of the heart is reported for both scurvy and beri-beri in terms which leave little doubt that essentially the same condition is being described (35). Vedder (36) points out striking similarity in the nervous symptoms observed in scurvy, beri-beri and pellagra, and notes that there are certain resemblances in their symptomatology and pathology.

240. **Two or More Deficiency Diseases Doubtless Frequently Occur Together.**—In the light of the description which has been given of the dietary properties of our more important natural food-stuffs and the products manufactured from them, it is interesting and instructive to estimate the deficiencies of typical diets which have been described as having occasioned numbers of cases of the so-called deficiency diseases. Thus, in the Burma prison, there was an epidemic of scurvy with the following dietary (37):

	Oz. Daily.		*Oz. Daily.*
Rice (husked)	24	Condiments	0.125
Beans	4	Fish paste	0.5
Vegetables (kinds not specified)	10	Salt	0.25
Oil (vegetable)	0.5		

In Southern Rhodesia, extensive epidemics of scurvy occurred in mines where the men were allowed the following foods (38):

Mealie meal (milled maize)	2 lb. daily
Meat	1 lb. weekly
Beans	2 lb. weekly
Monkey nuts	1.5-2 lb. weekly
Salt	ad lib.

Chamberlain (39) in 1910 observed that among 5,000 Philippine Scouts there were always from 100 to 600 incapacitated with beri-beri. Their diet had consisted of the following foods:

	Oz. Daily.
Beef	12
White flour	8
Potatoes or onions	8
Polished rice	20

On changing the diet by substituting 16 ounces of unpolished rice and 1.6 ounces of beans for the twenty ounces of polished rice, and including 20 ounces of sweet potatoes, the number of cases of beri-beri had fallen off by the end of 1910, to fifty. The following year there were three cases; in 1912 but two, and no cases in 1913.

241. **Comparison Between Diets Which Induce Beri-Beri or Scurvy, with Those to Which Pellagra Has Been Attributed.**—Voegtlin (40) selected the following diet (Diet A) for one hundred patients in the Pellagra Hospital at Spartanburg, S. C., who were suffering from mild and uncomplicated pellagra. He regards this as typical of the food supply of numerous homes where cases of pellagra are observed.

Diet A		Diet B	
Wheat bread	300 grams.	Wheat bread	300 grams.
Butter	30	Butter	45
Cabbage	100	Corn meal	50
Corn meal	50	Eggs	100
Ham	25	Meat	100
Hominy	75	Orange juice	100
Corn syrup	30	Potatoes	150
Pork	50	Prunes	30
Potatoes	150	Sugar	40
Prunes	30	Milk	1000
Turnip tops	100		
Sugar	40		
Milk	40		

Patients restricted to Diet A failed to improve or grew noticeably worse. They were later changed to Diet B, which differed essentially in containing much more milk, meat and eggs. Most cases showed definite improvement within two weeks, and within two months or more they were pronounced cured, except in a few more severe and advanced cases. The therapeutic value of the dietetic treatment was very spectacular.

Goldberger and Wheeler (41) undertook to determine whether adherence to a diet composed in great measure of milled cereal products, sugar, syrup, potatoes and fat meat would cause pellagra to develop in man. This was tested out on eleven healthy adult men in the Mississippi state prison in 1915. The men volunteered to submit to the test for the reward of pardon after six months' adherence to the experimental diet.

The following list of foods with their amounts, representing the diet per man per day for the week ending September 13, 1915,

is typical of the diets employed with a view to the experimental production of pellagra in man:

Corn meal	253.0 grams.	Sweet potatoes	100.0 grams.
Grits	38.7	Turnip greens	7.3
Corn starch	34.0	Cabbage	10.7
Wheat flour	150.3	Collards	24.6
Rice, polished	19.8	Pork fat	112.2
Cane syrup	27.3		
Cane sugar	57.8		

This was regarded as comparable in its constitution and quantitative relations with diets taken by pellagrins. With this diet Goldberger secured results which leave little room for doubt that men confined to it for a period of six months developed incipient signs of pellagra (41).

It is impossible to say, from a study of these diets why the two first mentioned should produce scurvy rather than pellagra. This is especially true of the diet of the miners of Rhodesia. It seems equally remarkable that the diet reported by Chamberlain caused beri-beri rather than pellagra, for so far as one can judge from the results of feeding experiments with animals, there are no special qualities in beef which could differentiate it from other foods in respect to any dietary essential which we should have reason to believe would induce a specific syndrome. The possibility is not excluded, of course, that pellagra is a disease which cannot be produced in those species of experimental animals which have been employed, because of the presence of synthetic powers of a specific type not possessed by man. The proof that the rat and prairie dog on certain diets can synthesize the antiscorbutic substance, affords an illustration of a case where this is true.

242. **Appleton's Observations on the Diet of Newfoundland and Labrador.**—Appleton (42) has contributed valuable data relating to the character of the diet of the people of Labrador along the Straits of Belle Isle, and also observations on the relation of the faulty food supply to the incidence of deficiency diseases. Under their dietary practises beri-beri, scurvy, edema and ophthalmia of dietary origin are of fairly common occurrence, and Dr. Appleton reports a single case of pellagra. This last observation is of extraordinary importance, for it is very unlikely that the patient should have been exposed to the disease, and its occurrence in this isolated region in sporadic cases, would seem to support the view that it is a deficiency of some kind in the diet which produces it.

The striking thing about Appleton's report, is that sometimes one and sometimes another of the deficiency diseases develops among people whose diet is so similar in different households. The entire population is evidently in a state of extreme nutritional instability, and small deviations of the constitution of the diet determine which disease will appear. The following table gives the approximate consumption of their principal articles of diet.

Bolted wheat flour	1¼ to 1½ barrels	per person per year.
Salt meats, pork or beef........	1 or 2 barrels	for a family of eight.
Salt codfish	2 to 4 quintals	" " " " "
Salt herring	1 to 3 barrels	" " " " "
Molasses	160 gallons	" " " " "
Potatoes	1 to 2 barrels	" " " " "
Rutabagas	1 to 2 barrels	" " " " "
Dried peas	20 to 40 gallons	" " " " "
Raisins	10 to 20 pounds	" " " " "
Butter substitute	160 pounds	" " " " "
Condensed or evaporated milk.	From a few tins to two cases.	
Tea	20 to 40 pounds per year for family of eight.	

Meat, salt fish, potatoes and dried peas are eaten only once or twice a week and the supply may become exhausted in April. Game is scarce and is little eaten. Fresh trout, cod and salmon are caught only during the summer. Small quantities of rice, onions or dried beans are occasionally secured, but only rarely. Gardening is little practised, but in favorable seasons enough cabbage may be grown to last until November. Poultry are not kept as a rule and egg powder is imported only in sufficient amounts for making cakes for fêtes. The only fresh fruit ever eaten are partridge berries and another little yellow berry called locally "baked apple." Tea is consumed in enormous amounts, ten to eighteen cups a day being not unusual.

243. **The Dietary Deficiency Diseases Must Occur Rarely in Man in the Uncomplicated Forms.**—The specimen diets which are given above have another meaning aside from that just discussed. They show that on any of these diets a man would not suffer from a single deficiency, but from several, and that where scurvy was observed it seems evident that there must have been likewise a serious shortage of the anti-neuritic substance, and consequently a tendency for symptoms of neuritis to develop. Furthermore the diets listed are all decidedly deficient in one or more inorganic elements, notably calcium. In these diets

poor in meat there was likewise a serious shortage of phosphorus as measured by the requirements of the rat.

It seems extremely probable, therefore, that in many instances where one of the diseases, beri-beri or scurvy, is diagnosed, the other exists as a complicating condition. This would account for the points of similarity in the manifestations of the two diseases as they have been described by several observers. It also raises the question as to whether the specific effects of lack of the anti-scorbutic substance or of the anti-neuritic substance, the remaining components of the diet being of optimal quality, can be said to be fully known, at least in the human subject.

244. The Prevention of Deficiency Diseases Does Not Necessarily Insure Good Nutrition.—It should be emphasized, finally, that the addition to such a diet as is ordinarily observed in the Orient to produce beri-beri, of some article of food which will prevent the development of beri-beri, will in many instances not go far toward correcting inorganic faults. From the standpoint of public health, therefore, it is by no means sufficient to prevent beri-beri in those countries where it occurs. This may be effectually accomplished, and yet the population may still be inefficient physically, and suffer from high infant mortality because of the poor quality of the mother's milk, and the adult members of the population may still early develop signs of senility. These statements are made on the basis of the assumption that the same physiological limitations with respect to nutrition, which apply to animals apply with equal force to man, and that these run parallel when the comparison of an animal with a man on the same diet is made on experiments covering equivalent fractions of the average span of life of which each is capable.

245. Borderline Malnutrition, Not Causing Alarm, of Greater Aggregate Importance Than Deficiency Diseases.—The data presented in this chapter, relative to the character of the diets of several groups of people in relation to the types of nutritive disaster which overtook them, serve well the purpose of illustrating the soundness of the proposition which is emphasized throughout this study of the relation of man's diet to physical well-being, viz.: the danger to health in the adherence to a diet in which milled cereal products, sugar, syrup, tubers and meats of the muscle type predominate. Such a diet is unsafe to a degree which makes it a matter of national importance.

It is especially important that the public be educated to a realization of the danger of poor physical development, poor

teeth, low health standards, physical inefficiency and early aging, which such a type of diet is sure to bring about. The alarming increase in the incidence of malnutrition among children, and the need for dental repair, together with the train of ills from which the present generation of adults is suffering, and which may safely be traced to faulty development and bad teeth, are in great measure the result of the poor quality of the diet of expectant and nursing mothers and of children. It will be apparent from what has been said, that it has become the general custom in many parts of Europe and America, to adhere to a diet which is but little better than those which in restricted areas are actually producing clinically recognizable diseased conditions. General observations should convince anyone that we are now, as a nation, falling far short of the physical perfection which would result from an improved dietary.

The observations of McCarrison afford very suggestive evidence that nutritive disturbances referable to faulty digestion with their far-reaching consequences for the health of the individual, are to be referred to borderline malnutrition brought about by food which does not meet the nutritive needs of the body. Our present living habits are characterized by too great consumption of bolted flour, degerminated cornmeal, breakfast cereals, and other seed products, tubers and muscle meats. We are taking too little of the protective foods, milk and the leafy vegetables, and a movement toward stimulating the consumption of these classes of foods, would go far toward effecting that improvement in our national health standards, for which the many agencies concerned with the public health are seeking.

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CHAPTER X

THE CHEMICAL NATURE OF THE ANTI-NEURITIC SUBSTANCE, WATER-SOLUBLE B

246. Schaumann's Views on the Nature of the Anti-Beri-Beri Substance.—In the preceding chapter it was described how Schaumann, who was the first to extend the suggestive studies of Eijkman, attempted to identify the substance in rice polishings, which effects a cure of polyneuritis or experimental beri-beri in pigeons. He observed that polished rice has a much lower phosphorus content than unpolished, and that the polishings which are extremely rich in this element are highly effective in preventing or curing the disease. These facts led him to suggest that the substance under investigation was of the nature of a nucleic acid. Nucleic acid is a substance occurring in the nuclei of all cells of animal and vegetable origin. It is an organic complex composed of four organic bases, four molecules of sugar and four molecules of phosphoric acid. This view he later abandoned when he was able, in 1912, to isolate from rice bran a phosphorus-free substance which would save from death, pigeons suffering from polyneuritis. He suggested that it functioned in a manner analogous to an enzyme, and since it was closely associated with the areas in the rice kernel in which phosphorus is abundant, he believed that it had some relation to the deposition of phosphorus.

247. Funk's Studies on the Isolation of "Vitamine."—Funk (1) made the first elaborate effort to isolate and identify the anti-beri-beri vitamin. He found that alcohol would extract a part of the physiologically active substance from rice polishings but that water was a far more effective solvent. From such solutions it can be precipitated by phosphotungstic acid or by silver nitrate and barium hydroxid, and also partially by mercuric chlorid. By means of the systematic procedure ordinarily employed for the separation of mixtures of organic bases, Funk established the fact that the curative substance contains nitrogen and is free from phosphorus. He believed at one time

that he had definite evidence that it belonged to the class of organic compounds known as pyrimidins.

It has been the experience of all investigators that the farther the substances possessing curative properties are purified, the less effective they become. This suggests that the important substance sought is not a crystallizable body, and that the crystals of definite and identifiable compounds thus far obtained are merely contaminated with the nutritive principle.

248. **Other Suggestions as to the Nature of the Anti-Beri-Beri Substance.**—The preparation described by Suzuki, Shimamura and Odake, and called by them oryzanin was certainly not a distinct compound, but a relatively complex mixture of substances extracted from rice polishings (2).

Edie, Evans, Moore, Simpson and Webster (3) obtained an active fraction from yeast, which they regarded as belonging to the pyrimidin group. This preparation they termed torulin.

Williams and Seidell (4) prepared a sample of adenin from yeast, and found that it had curative properties for polyneuritis in pigeons, but these were lost on keeping. They attributed the change in the physiological effect of the adenin relative to its anti-neuritic properties to molecular arrangement. The loss of anti-neuritic power they attributed to the gradual passing over of an unstable compound into a stable form. Voegtlin and White (5) and Harden and Zilva (6) have been unable to confirm these observations.

Abderhalden and Schaumann (7) have published a paper in which they describe attempts to isolate the anti-neuritic substance from yeast. They introduced two new terms (eutonin and nutramin), but otherwise made no advance toward the solution of the problem of isolating the anti-neuritic complex.

Hofmeister (8) reported that he had isolated a substance which he identified as a pyrimidin, and which possessed anti-neuritic properties.

Funk and others isolated nicotinic acid from rice polishings. The idea has been expressed that this or some unstable modification thereof, is the anti-neuritic substance. Extracts of rice polishings prepared according to the usual procedure for securing the "vitamin fraction," have been observed to develop a pyridin-like odor. Furthermore, Drummond and Funk (9) noted that preparations which were capable of curing pigeons of polyneuritis always gave the characteristic blue color with the Folin-Macallum phenol reagent, indicating the presence of a substance or substances containing hydroxyl groups (10).

249. **Williams' Investigations on Hydroxy Pyridins.**—Acting on this clue, Williams (11) prepared certain α-hydroxy pyridins and tested them for anti-neuritic properties by injecting them into polyneuritic pigeons. A number of cures were effected. On keeping, these preparations lost within a few days all curative power. From these findings Williams drew the deduction that the substances underwent a spontaneous change from an unstable to a stable form and that the latter was inactive. By treatment of inactive preparations with alcoholic sodium hydroxid he found it possible to transform them into the physiologically active condition. From the method of manipulation and treatment, he was justified in assuming that he had in the active preparation the enol form of the substance. None of Williams' synthetic preparations had anything like the activity or certainty of action that is seen in extracts of certain natural foods. He was led to surmise that the pathological condition of polyneuritis is not due to a deficiency of a substance *per se*, but to a lack of a certain type of potential energy which only certain substances can supply. In other words, he suggested that it was the potentiality of isomeric change, in the substance administered, which produced the physiological effect of restoring function to a paralyzed bird. To this isomeric change, Williams attributed the instability of the vitamins of natural foods. He did not draw the conclusion that the anti-neuritic vitamin is a hydroxy-pyridin, but pointed out that the same type of isomerism is possible in bodies of entirely unrelated natures such as pyrimidins, purins and other heterocyclic compounds.

250. **Williams and Seidell's Activation of Adenin.**—In a later publication Williams and Seidell (4) adsorbed by means of fuller's earth the anti-neuritic substance from autolyzed yeast. They then extracted the active material from the inorganic earth by means of 5 per cent sodium hydroxid. This procedure was said not to cause in the substance a loss of anti-neuritic property. The extracted material was subjected to crystallization, but the crystals were found to be inactive and were identified as adenin, one of the purins. When adenin was treated with boiling glacial acetic acid, acetic anhydrid, dilute hydrochloric acid or sulphuric acid, or allowed to stand for some time in the presence of dilute mineral acids or heated to boiling with concentrated sulphuric acid it was reported to have acquired anti-neuritic properties.

The deduction drawn by the authors from their data was that "an isomer of adenin is the chemical entity responsible for the

characteristic physiological properties of the vitamin under investigation." It is difficult to understand why, after obtaining their adenin from yeast, in a manner well known to lead to a partial isolation of the anti-neuritic substance, and after identifying adenin as a component of the mixture prepared by their procedure, and after having denaturized the substance so to speak, and finally having treated it so as to confer upon it once more pronounced anti-neuritic properties, these investigators should have placed such a modest estimate upon the significance of their results. They stated that they regarded their work as "of chief interest not in its contribution toward establishing the composition or identity of this "vitamin," which may or may not be a unique compound, but in affording corroboration of the theory advanced that isomerism plays a determinative rôle in the physiological potency of vitamins." It would seem justifiable under such conditions to assume that adenin, existing in a peculiar modification in yeast, is probably either the sole, or at least one of the actual entities which exert the anti-neuritic effect.

In a later paper Williams (12) again has expressed the view that under certain conditions α-hydroxy pyridin may possess anti-neuritic properties. He attributed these properties to the existence of this compound in the form of a pseudo-betain, and suggested that a configuration conforming more or less closely to that of the betain ring was probably an essential characteristic of the anti-neuritic vitamin. It was pointed out that such a structure was possible in most of the simpler nitrogenous components of animal tissues, especially in the purin bases.

The anti-neuritic substance is relatively stable toward acids, but undergoes a change of some sort when treated with alkalies so as to lose its physiological value. Sullivan and Voegtlin observed this destructive effect of alkalies, and their observations have been confirmed by McCollum and Simmonds and others (12).

251. **Seidell's Silver Compound.**—Recently Seidell (13) has described a method for the preparation of a relatively stable silver compound of the anti-neuritic substance. He discovered that fuller's earth has the property of absorbing from its solutions the physiologically active substance which exerts an anti-neuritic effect. In this way it can be separated from certain other substances with which it is associated. From the fuller's earth the vitamin is extracted by barium hydroxid. The barium

is quickly removed from the resulting extract as sulphate and lead acetate is subsequently added as a precipitant. The excess of lead is removed as sulphid, and the filtrate from this precipitate is evaporated rapidly under diminished pressure to a small volume, when a white amorphous substance separates. This is found to be inactive and is, therefore, discarded. Evaporation is continued in a vacuum desiccator and several crops of the white substance are secured and removed. The solution, which possesses great anti-neuritic activity, is finally evaporated to a thick viscous mass which can be finally brought to dryness. The physiological activity of the dried residue is retained for many months.

When this material is dissolved in a small volume of water and treated with silver nitrate, there is formed a voluminous precipitate, which does not contain the anti-neuritic substance. This precipitate is removed. To the filtrate silver nitrate and ammonium hydroxid are added. These reagents form a second silver precipitate which contains the desired vitamin. The filtrate is practically free from it. This procedure appears to be a distinct step in advance in the purification of this most interesting principle.

McCollum and Kennedy (13) conducted experiments with pigeons designed to show the importance of fat-soluble A as a factor in the etiology of experimental beri-beri, and to determine whether definite evidence could be secured as to whether the growth essential water-soluble B, which had been demonstrated on rats, was identical with the substance, specific starvation for which leads to beri-beri in birds. Their data indicated that any extracts of natural foods which furnish water-soluble B in growth tests with rats likewise effected "cures" of beri-beri pigeons. They were able to demonstrate that fat-soluble A plays no rôle in the production of experimental beri-beri in pigeons. These authors also found that acetone, ethyl acetate and benzene can extract from wheat germ, rendered fat free by extraction with ether, the anti-neuritic substance. It is now known, however, that these solvents are extremely inefficient for this purpose, and that not more than traces of the active substance can be isolated by their use as solvents.

252. Robertson's Observations on Tethelin.—In this connection the work of Robertson (13) should be mentioned. He separated a crude lipoid fraction from the anterior lobe of the pituitary of the ox to which he gave the name tethelin. He car-

ried out extensive experiments on the growth of mice designed to show the effect of tethelin. There was offered no evidence that a definite substance was isolated, for no adequate attempt was made to purify the active principle which it was believed to contain. Furthermore, the substance was, in his experiments, superimposed upon a mixed diet of considerable complexity, which was adequate for the nearly normal nutrition of the mouse. It is not possible to intelligently discuss Robertson's results, therefore, in connection with the dietary problems which form the theme of this book.

253. **Myers and Voegtlin's Procedure for Isolating the Anti-Beri-Beri Substance.**—Myers and Voegtlin (14) report that they have been able to remove the anti-neuritic substance from autolyzed yeast by means of its solubility in olive oil or in oleic acid. They state that it is also soluble in acidified methyl alcohol, and can be extracted from unautolyzed (dry) yeast by this solvent.

It will be seen from the foregoing, that but little progress has been made in devising methods for accumulating considerable amounts of the anti-neuritic substance or for determining its identity. There are other confusing factors which enter into studies of this character and which are not generally appreciated. One of these is that the results of several investigators have indicated that compounds of several kinds, including purins, pyrimidins and pyridins, have induced at least temporary "cures" in pigeons suffering from polyneuritis. Still more recently Dutcher (15) has reported "cures" of pigeons as the result of administering such physiological stimulants as adrenalin and pilocarpin, both of which are absent from all ordinary foods.

254. **Harden and Zilva Fail to Confirm the Experiments of Williams and Seidell.**—Harden and Zilva (16) and Voegtlin and White (17) have attempted to repeat the studies of Williams and Seidell purporting to show that adenin and α-hydroxy pyridin can acquire anti-neuritic properties. In all their tests they found no evidence that these compounds exert any curative action on pigeons suffering from polyneuritis. McCollum and Koch (18) have attempted to induce growth in young rats on diets lacking only the anti-neuritic substance, but containing instead adenin, pilocarpin hydrochlorid or adrenalin. In no instance was there the slightest indication that the physiologically indispensable complex was supplied by any of these compounds.

McCollum and Simmonds (19) also tested thymus nucleic acid as a source of the anti-neuritic principle, but with negative results.

255. **McCarrison's Investigations on Beri-Beri in Birds and Mammals.**—A new conception of the pathology of polyneuritis and other "deficiency" diseases was introduced by McCarrison (20). The most striking manifestations of beri-beri are the loss of the coördinating powers of the muscles. The onset of the disease is generally preceded by the bird sitting with ruffled feathers, and with the appearance of illness. There is progressive weakness, and when disturbed there is a tendency for many pigeons to be taken with convulsive seizures in which they turn "cart-wheels" backwards at intervals until they die. In the acute type of the disease, many birds sit with the head greatly retracted. These symptoms generally led investigators to the acceptance of the view that the lesions in beri-beri were principally situated in the nervous system. The studies of McCarrison, however, reveal the fact that injury to the nerves is much less pronounced than injury to certain other tissues.

On examining pigeons restricted to a diet of polished and autoclaved rice, McCarrison observed functional and degenerative changes in every tissue of the body. The thymus, testicles, spleen, ovary, pancreas, heart, liver, kidneys, stomach, thyroid and brain underwent atrophy, the severity in his cases being in the order named. The adrenals suffered hypertrophy. This hypertrophy was associated with a proportionate increase in the content of the glands in adrenalin. Edema, he found to be invariably associated with hypertrophy of the adrenal glands. In other words edema seemed to be associated with an excessive production of adrenalin.

Inanition was found to give rise to a state of adrenal hypertrophy and to atrophy of other organs, the brain excepted, similar to that observed in birds fed solely upon polished rice, a diet deficient in all known uncharacterized food substances, very deficient in protein and in several essential inorganic elements.

More serious than nerve lesions were the gastric, intestinal, biliary and pancreatic disorders observed in birds as the result of a diet deficient in those factors inadequate in polished rice. Such deficient dietaries gave rise to congestive and atrophic changes in all the coats of the intestine, especially the duodenum; to lesions in its neuro-muscular mechanism; to impairment of its digestive and assimilative functions, and to failure of its

protective resources against bacterial infection. In guinea pigs restricted to a diet of oats and autoclaved milk, there were observed lesions of the digestive tract analogous to those seen in pigeons whose diet was limited to polished rice. Owing to the multiple deficiencies of the rice diet, it is not possible to decide from these experiments as to the specific effects of deficiency or absolute lack of a single dietary component. It is suggestive, however, that on a diet deficient only in respect to the anti-scorbutic substance, guinea pigs developed lesions, comparable with those found in birds with diets faulty in several respects.

McCarrison (20) further studied upon pigeons the effects of a diet of polished rice, butter fat and onions. This diet was deficient only in the anti-neuritic substance and in several mineral elements, especially calcium, phosphorus, sodium, chlorin and potassium. The iodin in the thyroid was probably sufficient to tide the birds over the periods covered by his experiments. The butter fat supplied the factor A; onions the factor C, the anti-ophthalmic and anti-scorbutic substances respectively. On this diet typical symptoms of polyneuritis promptly appeared, showing that onion does not contain appreciable amounts of the anti-neuritic principle. The addition of onion, of which the birds ate greedily, to polished rice, of which they ate sparingly, afforded some measure of protection against the damaging effects of a diet of polished rice alone, for atrophy of the bowel, although often considerable, was usually less marked than in birds on the rice diet alone. Congestion was less prominent, and the atrophy of the myenteron and of the elements of the mucosa, although usually considerable, were often comparatively slight. Two cases in twelve birds examined were encountered in which bacterial infection of the bowel wall had assisted in inducing profound deterioration of its structures.

In a considerable number of birds whose vitality was depleted as the result of the types of faulty diets described by McCarrison, the blood was found to be infected by *Bacillus suipestifer*, *Bacillus pyocyaneus*, or another organism not identified. He pointed out that systemic infection was rendered easier by the presence of the pathological processes existing in the intestine as the result of dietary deficiencies. Such invasion of the body was favored by the impaired production of digestive juices, by the malnutrition of the secretory cells owing to the continued congestion of the mucous membrane, by the increased leucocytic traffic in microörganisms between the mucous membrane of the

intestine and the blood, by the greater opportunity which the debilitated mucous membrane provided for the growth of micro-örganisms on its surface and within its substance, and to actual breaches of continuity in the walls of the bowel itself. The imperfect digestion of food in the upper part of the alimentary tract offering a favorable medium for the growth of bacteria, tended, by the production of unwholesome products, to further debilitate the mucosa, and to increase the prospects of invasion of the latter by microörganisms. In his experimental animals kept on diets deficient in several factors, among which a lack of the anti-neuritic substance was a prominent feature, McCarrison observed with comparative frequency the superaddition of intense bacterial invasion of the bowel walls upon the atrophic and congestive changes brought about directly by malnutrition. Infection of the blood from the bowel under such conditions would be expected and was repeatedly demonstrated by aërobic culture of the heart blood.

In guinea pigs restricted for a time to a diet of oats and autoclaved milk, McCarrison also observed localized, destructive changes in the mucous and underlying coats of the stomach and duodenum. These changes were manifest before the animals had developed any of the characteristic naked eye appearances of scurvy, and he regarded them as pre-scorbutic.

256. **McCarrison Points Out That the Nerve Lesions Are Less Severe Than Other Lesions.**—This investigator further pointed out that the nervous symptoms of polyneuritic birds may be rapidly ameliorated or recovered from and yet these birds may die as the result of the gastro-intestinal lesions. He emphasized that the rapid recovery from the nervous symptoms indicated that of all the tissues, the nerves are least affected as regards organic lesions by vitamin deficiency. Much more serious damage resulted to the intestine, and recovery from these lesions was correspondingly slow. The remarkably rapid disappearance of convulsive seizures, of astasia and of cerebellar symptoms, indicated clearly that specific fasting for the anti-neuritic substance was in some manner intimately concerned with the functioning of the nervous system. According to McCarrison, this may be an activation or energizing action on the nerve cells, or a necessary condition for the completion of the nervous current. Certain it is that in the absence of this substance, the nerve cells are incapable of normal activity, and when it is provided, normal functioning is reëstablished with

dramatic suddenness. McCarrison accepts the view, expressed by Bayliss, that the function of the anti-neuritic substance is that of a catalyst.

257. **Subminimal Provision of Uncharacterized Nutrients and Certain Diseases of Children.**—Subminimal provision of the uncharacterized nutrient principles, resulting in marked impairment of the neuro-muscular control of the intestine with consequent failure of the latter to transport its contents in a normal manner, the impairment of the assimilative, secretory and protective functions, McCarrison suggests as etiological factors in certain pathological states in human subjects which appear to be the counterparts of these experimentally induced states in animals. His views on this subject are very instructive.

Pigeons fed exclusively on a diet of polished rice frequently suffer from diarrhea, and this can be regarded as a symptom of vitamin deficiency, since it can in many cases be caused to disappear at once by the administration of alcoholic extracts of egg yolks. Diarrhea or colitis is almost a constant precursor or concomitant of "war edema," which, as has already been shown, is in all probability, due to the combined deficiency in the diet of protein and anti-neuritic substance. At least this fact is true in the wet form of beri-beri. Continued subminimal dietetic deficiency of certain sorts may lead to a state of chronic gastro-intestinal catarrh, which characterizes those conditions in which mucus in abnormal amounts is produced by the intestine. Mucous disease is very common among European children in India who are fed largely sterilized milk, artificial foods, white bread, polished rice, poor butter, over-cooked vegetables and excessive quantities of sugar. Therapeutic experience has shown that this malady yields to a rationally selected dietary. The mucous stools, the diarrhea, the marked irritability, the unhealthy appetite rapidly disappear on such a regimen, as do also the "night terrors" from which such children frequently suffer (McCarrison).

In the category of syndromes caused by protracted feeding children on insufficient diets, McCarrison also ventures to suggest "celiac disease," described by Still (21). It is thus characterized: "Absent in breast-fed children, its onset between the age of nine months and two years, the diarrhea which so frequently precedes it, the cessation of growth, the ill-formed, pale, 'oat-meal stools,' the frequent association of scorbutic symptoms, the abdominal distention, the afebrile nature of the malady, the diminished size of the liver, the blood changes, the occurrence

of edema, the thin bones, the muscular feebleness—all these find their counterpart in pigeons fed on an exclusive dietary of autoclaved milled rice."

Again, McCarrison draws a parallel between the conditions observed in animals restricted to faulty diets of the types employed in his experiments and the anatomical factors seen in chronic intestinal stasis. Keith (22) regards defective action on the part of the abdominal musculature, and a lesion of the neuro-muscular system of the intestine, as the two factors of primary importance in the causation of this condition. Defective diet is certainly one means by which both the abdominal musculature and the neuro-muscular system of the intestine may be simultaneously impaired in functional capacity.

It must be kept in mind that McCarrison is hardly justified in speaking so unqualifiedly of "vitaminic deficiency" as the cause of the lesions observed. The extensive studies of McCollum and Simmonds and their co-workers have clearly shown the serious consequences of deprivation of certain of the essential mineral elements, notably calcium and phosphorus. McCarrison's diets were almost without exception, greatly deficient in several inorganic elements, including calcium, phosphorus, sodium and chlorin, and apparently contained a decided excess of acid over basic radicals. Deprivation of chlorin quickly leads to inability of the stomach to secrete hydrochloric acid, and this alone would seriously interfere with digestion, and with the suppression of bacterial growth in the alimentary tract. Diets deficient in mineral salts to the extent true of a diet of polished rice, of rice and butter, or of rice, butter and onion, might well lead to a state of depletion of the alkali reserve in the blood. Such deficient diets may account for the air hunger which he attributed to acidosis brought about by acid of fermentation resulting from a diet too largely derived from carbohydrate. It is scarcely safe to attribute all the observed symptoms in his experimental animals to deficiency of the uncharacterized dietary essentials. The conditions which he described are, however, induced by dietaries of a type which is at the present time exceedingly common in Europe and America. Putting aside minor details which may require revision, the conclusions of McCarrison represent an important advance in our understanding of the relation between faulty nutrition of a certain type and physical deterioration.

258. **McCarrison's View of the Relation of Nuclear Nutrition to Deficiency Diseases.**—McCarrison regards the term

"polyneuritis" as applied to the morbid state resulting in pigeons from an exclusive dietary of autoclaved rice as a misnomer, since it suggests that the nervous tissues are exclusively or mainly involved in the pathological process, whereas no organ or tissue escapes injury under such a dietary regimen. The glandular organs and the organs of digestion are more seriously damaged than is the nervous system. The morbid state resulting from (among other things) lack of what has been called the anti-neuritic vitamin, is not in reality a neuritis, and the term "anti-neuritic" is inaccurate. He regards the term "vitamin" inapt. He conceives the nutrient principles in the class which now generally passes under this term as "certainly nuclear ingredients essential for the nutriment of the living nucleus. They are 'nuclear nourishers' without which multiplication of cells does not occur. The term *nucleopast* (that which feeds the nucleus) might well be applied to them."

259. **The Relation of Appetite to the Intake of Water-Soluble B.**—With a view to discovering the peculiar rôle of the anti-beri-beri substance in metabolism Karr (23) studied the effect of specific fasting for this substance upon the desire of dogs to take food. He fed diets which were free from all three well recognized vitamins, and which were composed of isolated food substances, except that commercial casein and wheat gluten were employed as sources of protein. The dogs were restricted to these diets until they refused to take the food. Then a source of the anti-neuritic factor was also allowed them, and was fed separately. Yeast, milk, tomato, and a concentrated extract of water-soluble B were employed for this purpose. It was found that the addition of these substances to the diet resulted in prompt response of the appetite, the animals showing an increased desire for food. Karr concluded that there was some relation between the desire to partake of food and the amount of water-soluble B ingested. Brewery yeast was found much more effective than bakers' yeast for this purpose.

He further studied the metabolism of dogs deprived of water-soluble B, by making quantitative studies of the assimilation of nitrogen from the alimentary tract. No decrease in capacity for digestion, nor in the character of the metabolic products eliminated could be detected as the result of specific starvation for this substance.

260. **We have No Knowledge of the Chemical Nature of the Anti-Beri-Beri Substance.**—The view of McCarrison that

the anti-neuritic substance (his nucleopast) is closely concerned with the functioning of the nucleus would derive support from the early attempts of Funk, Williams and others to identify the anti-neuritic substance with purins or pyrimidins, since these are cleavage products of nucleic acids. It has been pointed out how, in recent times, all such views have received a setback, through failure of later investigators to confirm the observations recorded with hydrolytic products of nucleic acid. McCollum and Simmonds (19) have found thymus nucleic acid unable to replace in a diet, otherwise satisfactory, extracts which contain the substance water-soluble B, which nearly all students in this field now regard as identical with the anti-neuritic substance. It can hardly be regarded as satisfactorily demonstrated that the so-called vitamins are associated with the nucleus rather than with some other cell structure.

261. **Beri-Beri Does Not Appear in Fasting Birds.**—Funk (24) made observation that the symptoms of beri-beri did not appear in fasting birds and that an increase in the amount of food ingested, especially of carbohydrate, hastened the onset of the disease. Others have corroborated these findings. Dutcher (15) is of the opinion that the carbohydrate effect is due to an overloading of the oxidative mechanism of the body rather than to a specific relation between the metabolism of carbohydrate and "vitamin," the latter being used up in the process. Funk and Schönborn (24) found an increased sugar content in the blood to result from lack of the anti-neuritic substance, and a diminished amount of glycogen in the liver.

262. **Dutcher's Studies on Catalase in Beri-Beri.**—Dutcher believes that the anti-neuritic substance functions as a metabolic stimulant. He observed (25) that the body temperature fell during the development of avian polyneuritis and rose after the administration of the anti-neuritic substance. Measurement of the catalase content of the tissues of birds suffering from the disease, revealed the fact that catalase is decreased to 56 per cent of the normal, and that it returns to normal when they are treated with suitable extracts of natural foods. These findings, he interprets as a great reduction in polyneuritis of the oxidative processes of the body. It is pointed out that such a depression of oxidation resulted in the accumulation of toxic metabolic products, which affected the nervous system and brought about the typical paralysis and other symptoms.

263. **Glyoxalase in Health and in Experimental Beri-Beri.**

—Findlay (26) has reported a study of the effect of deprivation of pigeons of the anti-beri-beri substance, water-soluble B, on the content of glyoxalase in their tissues. Glyoxalase is an enzyme which plays an important rôle in the metabolism of carbohydrate. It has the power to transform "glyoxals" into lactic acid. The "glyoxal" which serves in the animal body as the intermediate substance between glucose and lactic acid is known as pyruvic aldehyd. Glyoxalase is more abundant in the liver than in other tissues.

Findlay observed that the amount of glyoxalase in the livers was reduced to about half the normal amount when the birds were caused to develop beri-beri through restricting them to a diet of polished rice. On inducing a "cure" by the administration of the anti-neuritic substance the amount of glyoxalase rose rapidly to two-thirds of the normal amount (26).

264. Catalase Studies Appear Not to Relate Directly to the Deficiency Disease Problem.—The studies made by Burge (26) of the catalase content of the tissues of several species of animals (goose, pigeon, sparrow) indicate, however, that this may vary in individuals of the same species and of similar weights and in a normal nutritive condition by as much as 100 per cent or more. It seems questionable, therefore, whether one is justified in attributing much significance to change in the catalase content of the tissues of animals as an index to their capacity for oxidation. The fall in temperature is, perhaps, but one sign of failure of the metabolic rhythm caused by lack of an indispensable substance, just as it may be expected to fail when the living tissues run out of anything essential for their proper functioning. According to Stehle (27) the variation in the catalase content of the blood and tissues is satisfactorily explained as being due to variation in the number of red cells present. He regards this test as of no significance as a measure of the extent of biological oxidations, and expresses the view that there is no relation between the latter and catalase values.

In the light of these facts, it must be admitted that we have no knowledge whatever of the nature of the rôle the anti-neuritic substance plays in metabolism. We do know that in its absence the metabolic processes fail, and that this failure involves not primarily the nervous system, but all the tissues of the body, the brain and nerves being injured least of all. The suggestion of Dutcher, that under conditions such as result from specific fasting for this substance, the accumulation of incompletely

metabolized products, may affect the nervous system and account for the striking loss of function, seems a probable one.

We have already mentioned the fact that the chemical nature of the substance or substances lacking in the diets which induce the syndrome generally designated as polyneuritis, is entirely unknown. Furthermore, we have no test for its presence or absence, other than a properly planned feeding trial in which a basal diet is employed known to be entirely satisfactory except for this one nutritive principle. The test animal is fed exclusively such a diet, to which is added a definite quantity of a natural food, or of an extract to be tested for the anti-neuritic factor. The success or failure of the nutrition of the animal will turn upon the presence or absence in the food or extract of the dietary principle in question.

265. The Pigeon Test for the Anti-neuritic Substance Is Unsatisfactory.—We are now ready to appreciate the misleading nature of the test which many investigators have employed in their efforts to determine the relative values of different foodstuffs, or of preparations made with the object of isolating and identifying the anti-neuritic substance. For this purpose the procedure of Funk has been almost universally followed. This consists of feeding pigeons on a dietary of polished rice until acute symptoms of impaired functional activity of the nerve cells appear. The substance to be tested is then administered and the recovery of the bird's powers of locomotion interpreted to indicate that the anti-neuritic substance has been made available—in other words that the test is positive. Failure of the bird to respond to this treatment is accepted as a negative test for this vitamin.

It was pointed out in 1918 by McCollum and Simmonds (28) that this test is inadequate and misleading, but no attention has as yet been paid by other investigators to this criticism of the classic "vitamin test." At that time they accepted the prevailing view that nerve degeneration was the most pronounced lesion in avian polyneuritis, and emphasized the probability that substances of a stimulating nature might whip up motor nerve cells which had lost their functional capacity, and might temporarily restore the birds to an apparently normal condition. They pointed out the high degree of improbability that so many totally unrelated chemical substances as pyrimidins, purins, and pyridins could fulfill the same physiological rôle. They were led to suspect that the "curative" substance was not, in

some cases at least, identical with the indispensable nutritive principle, essential for growth and normal functioning, but rather bodies which possessed the pharmacological property of goading to renewed activity, nerve cells which had been injured and had ceased to functionate. The observations of Uhlmann (29) and of Dutcher, made later in the same year, that pilocarpin and other physiological stimulants are actually able to induce "cures" of pigeons in polyneuritis, supports this view. The findings of McCarrison, that the nervous symptoms in avian beri-beri are of secondary importance, further emphasizes the rationality of the view that the pigeon test, as ordinarily carried out, is utterly without value for the specific purpose for which it has been so widely employed.

266. **Test for the Anti-Beri-Beri Substance Proposed by McCollum and Simmonds.**—McCollum and Simmonds described a test procedure which is infallible as an indicator for the presence or absence of the anti-neuritic substance. The procedure is to restrict young rats to a diet consisting of purified protein, dextrin, a suitable salt mixture, and butter fat or other fat which contains the factor, fat-soluble A. On such a food supply the animals are unable to grow, and ultimately die with or without the development of acute symptoms characteristic of polyneuritis. After a period of two or three weeks there is added to such a diet, a substance to be tested for the so-called anti-neuritic substance. If the animals recover their normal nutritive condition and *resume growth*, the test is positive. If the animals continue, however, to decline the substance tested for is absent from the material under investigation or is present in amounts too small to meet the nutritive needs of the subjects of the test. It is time that those who are devoting their efforts to the isolation and identification of this most interesting substance should adopt the above described test with a mammal. Until this is done we may expect no further progress in this direction.

Unfortunately this test requires moderately large amounts of material of a nature which it is laborious to prepare. Besides a considerable period of time must elapse before the outcome of such test becomes apparent. There is no chemical test yet discovered which in any way assists us in following up the physiologically active substance in our attempts to isolate it. Funk called attention to the fact that his active preparations (tested on pigeons) never failed to give with the Folin-Macallum re-

agent a test for the phenol group and Voegtlin has extended the use of this reaction in his efforts to isolate the anti-neuritic substance. This reaction is given by proteins, and by a very large number of organic compounds which are regularly met with in biological work, and has, therefore, no specificity, and can hardly contribute toward progress in the further investigation of the problem of the nature of this substance.

267. **Attempts to Employ Yeast as the Test Organism in Testing for the Anti-Beri-Beri Substance.**—Williams (30) brought forward a test for the anti-neuritic principle which at first appeared to be a great step in advance since it promised to detect very small amounts of the substance in a short space of time and with a minimal requirement of material. The test was based on the conception that the yeast cell is unable to grow in a medium lacking in the anti-neuritic substance. It was reported that the growth was in proportion, roughly, to the amount of "vitamin" present. The test was carried out with a hanging drop of culture medium. The number of progeny of a single yeast cell counted after an interval of a few hours constituted the basis of judgment as to the richness or poverty of the solution in the desired substance. Bachmann (31) also described a modification with yeast as the test organism, and Funk (32) described a method for growing larger numbers of yeast cells and measuring their volume by centrifuging in capillary tubes. Unfortunately, this method, which was hailed with great enthusiasm when first described, has proven to be a complete disappointment.

268. **Yeast Test Proves Disappointing.**—Souza and McCollum (33) attempted to make use of yeast cell growth as a test for the anti-neuritic principle (water-soluble B), and showed that no confidence could be placed in it. In the first place, it was found that yeast could grow slowly in a "vitamin"-free medium, and in the second place that the addition of extracts of natural foods which had been so treated as to destroy the anti-neuritic substance completely, were just as effective in stimulating the growth of yeast as were other extracts which did contain the dietary principle. MacDonald and McCollum then carried out an extensive series of transplantations of pure cultures of yeast in a nutrient medium containing no trace of water-soluble B (34). As a result they showed conclusively that a steady growth, through many successive seedings, is possible in the absence of the substance for which it had been suggested the growth of yeast could be made a specific test. Fulmer, Nel-

son and Sherwood (35), almost simultaneously published data fully in accord with that of Souza, MacDonald and McCollum, and drew the conclusion that the yeast test has no specificity whatever. We are, therefore, again thrown back upon the test for water-soluble B, described by McCollum and Simmonds, as the only one yielding results of any significance.

269. **Conclusions.**—It will be seen from the description presented in this chapter, that the methods and results used as a basis of investigation and of deduction, have been decidedly unfruitful in the knowledge which they have yielded of a food substance, about the existence of which there can be no question, and which is an indispensable complex for the living tissues. A field of great promise lies open here to the investigator, but we must wait until the efforts of the future have been directed along lines more logical and until investigators have viewed the problem in its proper perspective, before we shall see the successful solution of this most interesting problem.

In conclusion it appears that McCarrison is fully justified in his view that the condition commonly referred to as polyneuritis is actually not a neuritis, and the term anti-neuritic, is not descriptive of the condition to which it is applied. Degeneration of the nerves seems to be one of the later manifestations of the lack of the substance specifically concerned with the etiology of beri-beri. It would seem logical to discontinue the use of the term polyneuritis to designate the experimentally induced syndrome. In the light of McCarrison's findings the term "experimental beri-beri" is more fitting and proper.

Since the "cure" affected in tests with pigeons is actually not a cure, but merely an alleviation of one of the minor symptoms, it is obvious that the most appropriate, and most accurate conception of the subject should center upon the completeness or incompleteness of the diet with respect to a substance on a parity with an indispensable amino acid. The substance concerned with the etiology of this syndrome is apparently not an amine nor is it primarily anti-neuritic. While, for convenience, it is permissible to employ the term vitamin, with the spelling suggested by Drummond, it is most logical to use a term which has only an algebraic significance pending the acquisition of further knowledge of the chemical nature of the anti-beri-beri substance. For this purpose, the term water-soluble B appears even more appropriate, since McCarrison has published his studies, than ever before.

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CHAPTER XI

XEROPHTHALMIA (KERATOMALACIA)

270. **The Necessity of a Fat-Borne Vitamin in the Diet.**—In Chapter II it was shown that it is impossible to secure satisfactory nutrition in the rat without including in the diet certain fats containing a substance indispensable for the normal processes of growth or for prolonged maintenance of well-being. In the light of the history of science the researches relating to the necessity of certain lipins in nutrition are of great interest. The more significant investigations in this field will now be considered from the standpoint of the present day knowledge of what constitutes the normal diet, and emphasis will be laid upon the relation of deficient diets to certain states of malnutrition.

Stepp (1) while a student in the laboratory of Hofmeister at Strassburg, performed the first classic experiment in this field. Since every animal and plant cell contains certain substances having the physical properties of fats, in addition to proteins, salts, carbohydrates and water, to name only the substances of primary importance, Stepp believed that these fat-like bodies, the lipins, must be considered to be primary and indispensable cell components. Because most food-stuffs of animal or vegetable origin contain these lipins they occur regularly in our diet. What would happen if they were eliminated from an otherwise adequate food mixture? The answer to this question Stepp sought to obtain by a series of experiments on mice.

The group of substances classified as lipins includes fats and certain other compounds which have more or less similar physical properties. They have a greasy feel, and are soluble in one or more of such solvents as ether, alcohol, benzene, chloroform and acetone. The best known of these lipins aside from ordinary fats are lecithin, cholesterol, phytosterol, cephalin and the cerebrosids. Lecithin contains combined in its molecule glycerin, fatty acid, phosphoric acid and an organic base called cholin. Cephalin closely resembles lecithin, but yields on hydrolysis a different organic base, amino ethyl alcohol. Choles-

terol, chemically an alcohol, has certain physical resemblances to the fats. Cerebrosids are compounds containing in their molecules a fatty acid, a sugar (galactose) and an organic base (sphingosine). All of these are soluble in alcohol, but they differ in some extent in their solubility in the other solvents named. All of these substances play a prominent part in the composition of brain and nerve tissue.

271. **The Classic Experiments of Stepp on Lipin-Free Diets.**—Stepp prepared a bread made from milk and wheat flour, and another from milk and "protamol," a protein-rich preparation from rice. These he extracted thoroughly with alcohol and with ether. Mice were fed either the extracted or the unextracted breads. Those fed the extracted food died within thirty days, whereas those fed the untreated bread remained in good health during the six or eight weeks they were under observation. Stepp interpreted these results to mean that certain lipins (fat-like substances) are essential in the diet. He next sought to discover which of the individual lipins was indispensable for the maintenance of health.

The method employed was to restrict mice to the lipin-free diet (extracted) plus one or more of the individual lipins, the chemistry of which is more or less well understood, and which can be prepared in a state of purity. He tested out in this way lecithin, cholesterol, cephalin and cerebrosids, but in no instance was he successful in making the extracted diet complete by the addition of one or more of these purified substances. He also made an extract of egg yolk by shaking with cold alcohol, and divided the solution into two portions. One of these he heated with 95 per cent alcohol for two days in a water bath, while the other was heated long enough to evaporate the alcohol. Each of these preparations was added to a portion of the extracted bread and the two mixtures served as rations for two groups of mice. The group fed the heated preparation all died within thirty days, while the other group receiving the unheated preparation remained in good health. Stepp thus discovered that the substances which dissolved from his breads when they were treated with alcohol and ether were changed by heating during several days, so that they were no longer capable of rendering the extracted breads satisfactory for the nutrition of mice.

272. **A Comparison of Birds with Mammals with Respect to Lipin Synthesizing Powers.**—Stepp was led by the experiments of Fingerling (2) to investigate the problem whether birds

differ from mammals in their capacity to synthesize the complex lipins. It was shown by Fingerling, and simultaneously and independently by McCollum, Drescher and Halpin (3) that birds may be satisfactorily nourished on diets very poor in lipins of every kind. McCollum, Drescher and Halpin fed three half-grown hens exclusively on a mixture of polished rice and skim milk powder, the latter having been extracted with ether to render it essentially free from fats. On this diet the hens increased their body weights about 33 per cent, and laid 57 eggs. These eggs collectively contained 82.95 grams of lecithin and cephalin. This is several times the amount of these substances contained in the entire tissues of the hens.

Fingerling fed his ducks on a diet consisting of 300 grams cooked potatoes, 80 grams cooked blood albumin, 300 grams of boiled starch, 10 grams of calcium phosphate and 10 grams of calcium carbonate per bird per day. The ducks had completed their growth before the beginning of the experiment. One duck was estimated to have deposited in her eggs 302.3 grams of lecithin, another 246.0 grams and another 212.7 grams. The birds remained in good health during the egg-laying period. This diet would not have maintained them through a second laying period.

Stepp (4) sought to determine whether pigeons differ in their nutritive requirements from mammals. He fed three pigeons exclusively on dog biscuit which had been very completely extracted with hot alcohol. All were dead at the end of 43 days. The cause of death was polyneuritis, the analogue of beri-beri in man. Another pigeon restricted to the same food was unable to stand on the 38th day because of weakness and polyneuritis. It was then given doses of a commercial "vitamin" preparation (oryphan) plus an alcoholic extract of egg yolk to furnish the lipins which Stepp believed to be indispensable for mammals. The bird rapidly recovered and remained in good condition on this diet until the 92nd day of the experiment. It was then fed unextracted dog biscuit until the 98th day. The diet was then changed to extracted dog biscuit supplemented with the commercial preparation of the anti-neuritic substance (oryphan) but without the lipin extract. The body weight of the bird at this time was 271 grams. It had been observed on the experimental diets for 117 days. On this lipin-free diet it steadily, but slowly, lost weight so that by the 193rd day it weighed but 217 grams. It still ate well, but its flight was unsteady. Unex-

tracted dog biscuit was fed for two days. The pigeon was then given the extracted dog biscuit without the addition of either lipins or "vitamin." The result was a rapid loss in weight, and the development of symptoms of polyneuritis. Death occurred on the 233rd day.

From these observations Stepp drew the unwarranted conclusion that the bird does not require the indispensable lipins or substance which accompanies them, which he had demonstrated to be necessary in the nutrition of mice. The steady loss of weight of his pigeon when the lipin extract was omitted from the diet shows clearly that its nutrition during this part of the experiment was not satisfactory. These results do not warrant Stepp's conclusion that there is a difference in the nutritive requirements of birds and mammals.

273. **Element of Growth Was Not Included in Stepp's Experiments.**—It should be remembered that in Stepp's investigations the element of growth was not included. He studied the nutritive requirements for maintenance of mice and pigeons, whose growth was complete. His results are, nevertheless, of great interest because they agree with those McCollum and Davis obtained with growing rats (5). They established the fact that for the mouse and rat, two substances at least, other than the conventional components of the diet, protein, fat, carbohydrate and salts, are essential for satisfactory nutrition. Stepp, in his early studies, interpreted the results to indicate that only certain lipins were necessary to supplement successfully a diet of purified food substances of the hitherto recognized group. When Funk demonstrated the necessity of a protective "vitamin" for the prevention of beri-beri, Stepp extended his studies to include "vitamins" in addition to lipins. Finally, in November, 1915, he presented data showing the necessity of "vitamins" as well as certain other substances soluble in alcohol (6). These are present in many natural foods. McCollum and Davis simultaneously published a paper in which they demonstrated the necessity for growth in rats, of a fat-soluble and a water-soluble substance. It may be well at this point to call attention to the bearing of the studies of Stepp on the question whether there are any demonstrated differences in the nutritive requirements of mammals during growth as contrasted with those for maintenance in the adult.

274. **Drummond's View That Fat-Soluble A Is Not Necessary for Maintenance in the Adult.**—Drummond (7) holds the

view that adult rats need little if any of the dietary factor, fat-soluble A, for the maintenance of health. Stepp's observations indicate the reverse. McCollum and Simmonds (8) found, when the sole source of fat-soluble A was 33 per cent of millet seed in the food mixture, adult rats developed, after 60 days, severe xerophthalmia, although this seed contains demonstrable amounts of this dietary essential. It is possible that adults require somewhat less of this factor for normal maintenance than young animals do for growth, but this fact does not appear to have been proven. It is important to appreciate that an animal on a diet which is highly satisfactory in all respects other than in its content of fat-soluble A, will not show distinct signs of a lack of this substance for a much longer time than would be necessary to make the shortage apparent if a second factor in the diet were below the optimum in quality and quantity. The extent to which this second factor deviates from the optimum would determine the reaction of the animal, whether it would be prompt, or delayed in showing the effects of faulty nutrition. If at the same time there should exist a deficiency in a third factor, the effects of lack of fat-soluble A would become increasingly apparent. In the interpretation of quality in diet it is of the utmost importance to realize that there is an interrelation of factors, and that it is easily possible to overlook, in short experiments, deficiencies which are of small magnitude, but which, nevertheless, manifest themselves sooner or later in the life history of the individual.

Nearly all investigators in the field of nutrition have now accepted the view first formulated by McCollum and Davis (5) that two classes of unknown substances are necessary for the normal nutrition of the rat. The terminology by which McCollum and Kennedy (9) designated these as fat-soluble A and water-soluble B, has been widely adopted, because of its convenience, and because of the desirability of using algebraic terms to designate the substances in question until further investigations reveal their chemical nature. F. Röhmann, of Breslau, who has for many years studied the problem of nourishing mice on diets composed of *partially* purified food substances, refuses to accept the idea that there are any essential components of the diet which cannot be furnished by purified proteins, carbohydrates, fats and mineral salts, provided the proteins contained in the diet have an appropriate chemical constitution (10).

275. **The Experiments of McArthur and Luckett.**—McArthur and Luckett (11) misjudged as did Stepp in his earlier experiments, the peculiar nutritive value of butter fat as a source of an unidentified dietary essential. Stepp (12) added butter fat to a diet free from substances soluble in ether and alcohol, and observed that the mice in his experiments died just as early as they did on the lipin-free diet, whereas the same ration was made adequate by the addition of an alcoholic extract of egg yolk or calf brain. McArthur and Luckett did likewise. These investigators, like Stepp, drew the conclusion that butter does not contain an indispensable substance for the nutrition of the mouse. The explanation of their results was finally brought out by the studies of McCollum and Davis (5). When butter fat or an ether extract of egg yolk was added to a diet of purified food-stuffs, only one of the unidentified dietary essentials (fat-soluble A) was introduced. When an alcoholic extract of egg yolk was added, both fat-soluble A and water-soluble B were contained in the added material. Since the addition of either the factors A or B alone does not make a diet of purified protein, carbohydrate, fat and mineral salts complete, the animals fed such diets with but one addition died, and there was no evidence in the experiment to show that the butter fat had any special properties. It was difficult to discover that in the one procedure one essential substance, and in the other two, were being added, and that the presence of the two was the determining factor in the outcome of the experiment.

276. **Symptoms Resulting from Specific Starvation for Fat-Soluble A.**—When animals are restricted to a diet lacking in fat-soluble A, there develops after a few weeks a peculiar pathological condition of the eyes which is so characteristic that it must be regarded as one of the manifestations of a specific syndrome. It has not yet received from pathologists the attention it deserves. In 1909 Knapp (13) restricted rats to a diet of isolated and purified food substances, consisting of proteins, carbohydrates, fats and mineral salts, and described a severe conjunctivitis which developed as the nutrition of his animals failed. In other experiments lecithin, cholesterol and nucleic acid were added to the basal diet, and although the animals suffered from malnutrition and died, the characteristic eye symptoms did not appear. This is probably to be explained by the presence of fat-soluble A as an impurity in the lipins which he employed as additions to the experimental diet.

Freise, Goldschmidt and Frank (14), in 1913 observed the same eye disorder in their experiments with rats which they restricted to a diet similar to that used by Knapp. They described the condition in more detail than did Knapp. They stated that in about three weeks from the beginning of the experiment the eyelashes of the animals began to fall out. There was also a retraction of the eyeballs from spasm of the extrinsic muscles of the eyes. In five to six weeks the selerotic coat became dry, the cornea clouded and finally ulcerous, but without marked inflammation. The fur of the animals became rough. They succumbed to malnutrition, and histological examination of the sclerotic coat revealed the typical picture of keratomalacia as it is seen in man. In cases where the ulceration of the sclera of one eye was well developed, and was beginning to show in the other, the process could be entirely arrested by the administration, suggested by the work of Hopkins, of two cubic centimeters of skim milk per day. These workers believed that the condition developed only in young growing animals, and that it was closely related to the phenomena of growth. They attributed the condition to lack of "accessory" substances in the diet.

277. **Hopkins Experiments Demonstrating the Necessity of "Accessory" Food Substances.**—When Hopkins pointed out in 1912 that the addition of small amounts of milk to a diet of purified food substances would lead to growth, whereas without such addition the animals failed, and on the basis of this observation conceived the idea that certain "accessory" food substances are necessary in the diet, he had no comprehension, apparently, of the number or specificity of these substances. This view did not become appreciated until Funk attributed to specific deficiency a number of diseases, especially beri-beri, scurvy, pellagra, rickets and sprue, and expressed the belief that a special "vitamin" for growth was essential. The view that there were two unidentified substances essential in the diet did not become established on experimental evidence until McCollum and Davis (5) in 1915 published their paper on the essential factors in the diet during growth.

278. **Osborne and Mendel Describe Ophthalmia in Their Experimental Rats.**—In 1913 Osborne and Mendel (15) called attention to the prevalence of an inflammation of the eyes of their rats restricted to a diet of purified proteins, "protein-free milk," lard and starch. They referred to this as a "type of nutritive deficiency exemplified in the form of an infectious eye

disease prevalent in animals inappropriately fed," and stated that the condition was speedily alleviated by the introduction of butter-fat into the diet.

279. **McCollum and Simmonds Prove Xerophthalmia to be Due Specifically to Lack of Fat-Soluble A.**—McCollum and Simmonds had repeatedly observed the development of this peculiar form of ophthalmia in animals subjected to their experimental diets. They, however, did not feel convinced until they had collected numerous observations, all of which pointed to the belief that the eye disease in question is non-infectious, that it could more satisfactorily be explained on the basis of specific starvation for fat-soluble A, than on any other. Many groups of rats in various degrees of enfeeblement or arrested development resulting from restriction to faulty diets of various types, failed to develop the disease, when others in adjacent cages were suffering from it. They found it to occur only in those animals whose diets were faulty in the content of fat-soluble A. McCollum and Simmonds (16) correlated these observations on rats with those reported by Bloch and by Mori, and came to the conclusion that the xerophthalmia or keratomalacia produced experimentally in animals is the analogue of the condition which these authors have reported in man. It was on evidence of that nature that they formulated the view that this type of xerophthalmia is a deficiency disease in the same sense as beriberi, and that it is due specifically to lack of fat-soluble A.

280. **Mori Described Ophthalmia of Dietary Origin in Man as Early as 1904.**—The observations of Mori (17) mentioned above refer to about fourteen hundred cases of xerophthalmia among children between the ages of two and five years, which occurred in Japan in 1905-1907. These children exhibited keratomalacia as well as xerosis of the conjunctiva. This syndrome is known in Japan as hikan. Mori states that the disease does not occur among fisher folk, but among people whose diet is largely of vegetable origin. The children suffered from diarrhea in the summer time in addition to the eye lesion. The diet consisted of "rice, barley, cereals, beans and other vegetables." The nature of the other vegetables and the relative amounts of the different articles in the diet were not stated. Prompt relief of the eye symptoms was observed when cod liver oil was administered. Chicken livers and eel fat were also found to be effective as a remedy. The successful treatment of xerophthalmia in these children by the administration of cod liver oil,

or by the feeding of a glandular organ, such as liver, affords very strong evidence that the ophthalmia was the same condition as has been produced experimentally in animals, since it is relieved by the addition to the diet of fat-soluble A.

281. **Bloch Adds Greatly to Our Knowledge of Ophthalmia of Dietary Origin in Infants.**—Bloch (18) described fifty cases of xerophthalmia in children in the vicinity of Copenhagen that occurred during the years 1912-16. Most cases were infants under one year of age. They were suffering from severe malnutrition. The skin was dry, shriveled and scaly. Their diet consisted of separator skim milk, which was therefore practically free from fat. This milk had been pasteurized and then cooked again in the home before it was fed. Oatmeal gruel and barley soup constituted the other important ingredients of the diet. These infants were doubtless suffering from a complication of faulty dietary factors. Such a diet would contain relatively little fat-soluble A, the amount depending on the nature of the feed of the cows; the thoroughness of skimming; the amount of skim milk which was consumed by the infants, and the extent to which the heat treatment destroyed it. If the consumption of cereal was large, the amount of milk taken would be too small to insure a satisfactory inorganic content in the diet. Such a diet as Bloch describes would be practically free from anti-scorbutic substance. The infants which he observed may well have been borderline cases of both scurvy and beri-beri as well as well developed cases of xerophthalmia. *In the past we have failed to appreciate the seriousness of the condition of malnutrition which falls but little short of a deficiency disease.* The effects on vitality may be very pronounced in cases where a faulty diet is persisted in to a point where clinically observable symptoms are about ready to appear, but while no clear cut lesions are detectable.

Bloch referred the malnutrition in these infants to lack of fat in the diet, basing his belief on the observation that the eye trouble could be relieved by the administration of cod liver oil, whole milk or cream mixtures. In a sense he was right, but in the light of our present knowledge concerning the differences in the dietary properties of various fats, there is no reasonable doubt that vegetable fats such as olive oil, cotton-seed oil, soy bean oil, cocoanut oil, etc., would not have been of any therapeutic value. The prominence of skim milk suggested to Bloch the paucity of fat in the diet, and he fortunately chose two effective

fats, cod liver oil and butter fat, for administration to his infants. His generalization from the effect of these fats, to fats in general, was, we now appreciate, unwarranted.

282. Ophthalmia in Infants Generally Complicated with Scurvy or Other Deficiency Syndrome.—Malnutrition of a specific type rarely, if ever, occurs uncomplicated in man or animals living on a diet of ordinary food-stuffs, even when the list of foods available is greatly restricted and the diet unsatisfactory to a pronounced degree. The specific deficiency diseases, with the possible exception of scurvy, can be produced as uncomplicated syndromes, only by carefully planned experimental diets. This will be evident to one who considers the nature of the deficiencies of polished rice and of muscle meats, the prominent articles in the diet of those peoples in certain countries, who suffer most from beri-beri. Such a diet is deficient in mineral elements to a degree that would in time greatly lower the vitality and shorten life. Its content of fat-soluble A is so low as to produce a borderline, if not an actual condition of keratomalacia. The defect which produces the most prompt and most visible pathological picture is that resulting from the lack of the anti-neuritic substance. Beri-beri appears, and overshadows in the eyes of observers, all other features of general malnutrition.

In the reported cases of xerophthalmia in man, the inference seems justified that, although many of the infants were doubtless suffering from latent scurvy and under-feeding, lack of sufficient fat-soluble A was a prominent factor in their malnutrition.

283. Hess and Unger Express the View That Fat-Soluble A Is Not Very Important in Human Nutrition.—Hess and Unger (19) hold the view that in human nutrition there is not likely to be a deficiency of fat-soluble A sufficiently pronounced to be a factor of importance except under exceptional circumstances—as in times of war. They base their conclusion on an experiment conducted with five infants who were fed dried skimmed milk (Krystalak) 180 grams; sucrose 30 grams; cotton-seed oil 30 c.c.; autolyzed yeast 15-30 c.c.; orange juice and cereal. The autolyzed yeast was to insure a liberal supply of the antineuritic substance, water-soluble B. The orange juice was to supply the anti-scorbutic factor, water-soluble C, and the olive oil to furnish fat. The diet was assumed to be almost free from fat-soluble A, but entirely adequate so far as definite understanding of the necessary factors can be judged in the light of

present knowledge. The babies were from four to nine months old. They were confined to this diet for periods varying from five to nine months. Rickets was not observed in any of the babies. In fact they grew in a fairly normal manner. From this experimental data Hess and Unger were led to doubt whether more than traces of fat-soluble A are necessary in the nutrition of the human infant when other factors in the diet are satisfactory.

There is a fundamental weakness in their experiment. The assumption that the diet employed was nearly devoid of fat-soluble A, the factor on which the results were supposed to turn, is erroneous. Soon after the discovery of the existence of this dietary factor, McCollum and Davis (20) studied the relative values of the fat and non-fat portion of milk as sources of fat-soluble A. They compared the growth of young rats fed on diets of similar composition with respect to the several components. They made 3 per cent of butter fat the sole source of fat-soluble A in one diet and 10 per cent of skimmed milk powder (Merrell-Soule) in another. It was observed that growth and well-being were about equally well maintained in the two groups of animals. In 100 c.c. of whole milk there is approximately 3 grams of fat and 10 grams of solids not fat, and in the skimmed milk powder the fat was not more than 0.6 per cent. The 10 per cent of skimmed milk powder used in the one experiment, therefore, represented the same amount of milk as did the 3 per cent of butter fat. From this observation McCollum and Davis drew the conclusion that skimmed milk contains much more fat-soluble A than could be accounted for on the basis of its fat content. They expressed their belief that about half the fat-soluble A contained in milk is removed with the butter fat in skimming with the centrifugal separator, and half remains behind in the skimmed milk. If this observation is trustworthy, the diet employed by Hess and Unger was not very deficient in fat-soluble A, and indeed did for their infants just what it would have done for the nutrition of young rats—animals which respond very sensitively to a deficiency of this substance. Hopkins (21) has recently stated in a symposium on diet held by the British Medical Association, that he has observed experimentally the effects of skimmed milk as a source of fat-soluble A, and is also convinced that it contains much more of this

284. Urinary Calculi in Relation to Deficiency of Fat-Solu-

substance than its fat content would lead one to expect.

ble A.—A further abnormality attributed to deficiency of fat-soluble A in the diet was reported by Osborne and Mendel (22). They found in the urinary tract, calculi of calcium phosphate. In 857 autopsies they found calculi in 91 animals. Forty-three per cent of these had not had a satisfactory supply of fat-soluble A. Mendel (23) calls attention to the fact that urinary calculi are exceptionally common among peoples of the Tropics, and of the Far East, who live on diets quite unlike the mixed diets common among Europeans and Americans. He suggests a correlation of his experience with the well-known fact that these calculi are deposited from neutral or alkaline urines, which frequently owe their reaction to the formation of ammonia as a result of bacterial decomposition. The possibility that the invasion of the urinary tract by microörganisms results from the lowered vitality due to partial or complete starvation for fat-soluble A is suggested by their findings at necropsy. I am not greatly impressed with the view that there is any specific relation between starvation for fat-soluble A and the occurrence of calculi. Fifty-seven per cent of the animals found in the autopsies of Osborne and Mendel to contain calculi of the urinary tract had had a satisfactory supply of this dietary factor. In our own experience calculi have occurred so frequently in animals whose diets contained an abundance of this factor, but were faulty in other respects, that it would seem to be the result of general debility rather than lowered vitality brought about by specific cause.

285. Hemeralopia and Nyctalopia Possibly Associated with Vitamin Deficiency.—It is of interest in this connection to call attention to another widespread condition which seems related to a deficiency of fat-soluble A in the diet of man. Hemeralopia, or inability to see by subdued light, is common in several parts of the world, and has been frequently referred to faulty nutrition. Thus Krienes (24) attributed certain cases of the disease to malnutrition. De Gouvea (25) gave a résumé of the literature of the subject up to 1883, and described many cases of hemeralopia among the negro slaves who worked on the coffee plantations of San Paulo, Brazil. They were restricted to a diet of beans, pork fat and maize meal. Slaves on other plantations who were better fed did not suffer from the disease. Little (26) mentioned the prevalence of night blindness (nyctalopia, often inaccurately called hemeralopia) among the people of Newfoundland. He also stated that the diet was sufficiently poor

to make beri-beri and scurvy a common occurrence. I am informed by Dr. Grenfell that night-blindness is common in Labrador. Dr. Appleton, in a private communication also informs me that she has seen many cases of this eye disease in Newfoundland and Labrador. The diet of the inhabitants of these regions consists almost exclusively of bread made from bolted wheat flour, canned meats, fish, molasses, tea and small amounts of raisins.

The diet of these regions is of a character which one would expect to be dangerously low in its content of fat-soluble A as well as deficient in other respects. It is essentially a diet derived from the endosperm of wheat, muscle tissue of beef, pork and fish, and molasses. The last article of food, after its drastic treatment in the manufacture of sugar, would not be expected to have any appreciable value as a source of any of the unidentified dietary factors. Such a diet is actually so poor in the anti-neuritic substance that beri-beri is of frequent occurrence, and is likewise so poor in the anti-scorbutic factor as to make scurvy common. Judging from the known dietary properties of muscle meats, there is every reason to believe that the diet is also deficient in fat-soluble A. The regular use of cod livers as an adjuvant to the diet in these places is advisable, since this would prevent both beri-beri and scurvy, and perhaps also night-blindness.

Dr. Ann Young, who has had experience as a medical missionary in India, has informed me that night-blindness is common in the vicinity of Calcutta (27). The popular remedy for the condition consists in poulticing the eyes with an exudate of fresh goat's liver and in including liver in the food. I have also been informed from several sources that the value of liver for the cure of night-blindness has been appreciated in Japan from very early times. It has already been pointed out that the glandular organs of animals are good sources of fat-soluble A. It is not to be wondered at, if our surmise is correct, that night-blindness in certain parts of the world is in reality due to specific starvation for fat-soluble A. That it should occur in parts of India where the people subsist to a great extent on a diet derived from muscle meats and from those parts of the plants functionating as storage tissues is to be expected from our present knowledge of nutrition. Several types of faults in such diets would tend to predispose to susceptibility to lack of fat-soluble A. In Japan where there is no dairy industry, the supply of

fat-soluble A would depend largely upon the extent to which leafy vegetables are ingested. Certain edible roots have been shown to contain moderate amounts of this factor, but the amounts of such succulent foods as would ordinarily be eaten by man would scarcely suffice to meet the requirements of the body. The encouragement of the dairy industry in these countries, or the importation of liberal amounts of dried or canned milk, and their wider use in the diet, together with the utilization as adjuvants to the diet of fish livers and other glandular organs of animals, and of eggs, would go far toward the elimination of this disease, which, provisionally, may be regarded as a specific syndrome of dietary origin.

From early times records have come down to us showing that epidemics of dropsy have occurred during famines caused by drought or war. In the descriptions of this disorder, it has been noted that hemeralopia frequently preceded the development of the edema. It is said that night-blindness is endemic in Russia during the Lenten Fasts. Corneal ulcers and xerosis of the conjunctiva have sometimes been noted, among those who suffered from edema due to faulty nutrition, and ophthalmologists have repeatedly referred these eye changes to poor nourishment. These eye troubles in man result from conditions so complicated that it is not possible without further evidence, to attribute all of them to specific starvation for fat-soluble A. There is, nevertheless, a strong presumption that xerophthalmia or keratomalacia and night-blindness (hemeralopia, nyctalopia) not infrequently occur as manifestations of a deficiency of this dietary factor.

This conclusion is supported by the frequent occurrence in the literature of ophthalmology of expressions of the belief that malnutrition may bring about the condition of defective vision known as hemeralopia. Illustrations are found in the association of eye diseases with pellagra by Rampoldi (24), in the view of Saweljew, published in 1892, that night-blindness results from fat hunger (24); in the report of Roussanow (24) as early as 1885, that cod liver oil is an unfailing remedy for hemeralopia, and in the description of "springtime catarrh" and its associated conjunctivitis by Vetsch (24). These observations suggest that a diet derived too largely from cereal products, tubers and other foods having similar deficiencies, induce lowering of vitality, which becomes manifested, among other ways, in faulty vision.

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FIG. 11.—Illustrates a baby observed and treated by Dr. C. E. Bloch of Copenhagen. The child was suffering from severe xerophthalmia due to being confined too largely to a diet of separator skim milk supplemented with cereals. The right eye is filled with leucocytes and presents a yellow appearance. The left eye is swollen shut. The right eye was affected with a corneal ulcer. The sight of the right eye was lost.

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CHAPTER XII

CHEMICAL STUDIES OF THE DIETARY ESSENTIAL, FAT-SOLUBLE A

286. **Best Sources of Fat-Soluble A.**—There has been much interest shown among a group of chemists in the problem of determining the nature of the dietary essential, fat-soluble A, but little has been achieved in this direction. The history of the studies relating to this phase of nutrition is sufficiently interesting and instructive to warrant its inclusion as a special chapter. Biological tests have revealed the distribution of this dietary factor among our more important foods, and the relative abundance with which it occurs in a long list of articles of animal and vegetable origin is well known. Among the fats, the best sources are cod liver oil, butter fat and egg yolk fats. Some leaves of plants are known to be excellent sources, and there is good reason to believe that most of the unspecialized leaves (those not modified as storage tissues) contain it in relative abundance. In various parts of the world, grazing and browsing animals live exclusively or nearly so on the leaves of grasses or of trees, thus deriving their sole supply of fat-soluble A from this source.

287. **Distribution of Fat-Soluble A in Vegetable Foods.**—The early experiments of McCollum and his co-workers yielded results which seemed to warrant the generalization that, when estimated on the basis of the nutritive needs of the rat, all seeds, of plants, tubers and fleshy roots were decidedly deficient in this substance. This judgment rested on their observation that all foods they examined, which were functionally storage tissues of plants, could be enhanced in their dietary properties by the addition of butter fat. This generalization still appears to be justified, although with certain reservations which at that time could not be discerned. There is room for difference of opinion among students of nutrition concerning what constitutes an adequate amount of any dietary essential. One worker may make the basis of his judgment the ability of an animal to

grow in an apparently normal manner to approximately the full adult size and may thus be led to the belief that a certain intake of fat-soluble A is adequate. Another worker, planning his experiments so as to cover the entire life history of his animals, may find that the minimum amount of the factor in question which will just serve for the support of normal growth and the apparent maintenance of health during several months, is inadequate when the entire span of life is taken into account, and that a degree of deficiency which did not make itself apparent in the shorter period of observation is easily detected in the appearance of early deterioration and aging. The fertility may be affected as may infant mortality, or there may ensue defective development of the bones or teeth or both. Much depends upon the standards of the investigator concerning what constitutes "normal" nutrition. As will be pointed out in a later chapter, we have come to hold the view that "normal" is not a good word to use in nutrition studies. Optimal well-being, the best condition which can be reached, should serve as the standard of comparison.

288. **Yellow Maize Contains More Fat-Soluble A Than White Varieties.**—An extremely interesting observation was made by Steenbock and Gross (1) in 1919. They discovered that carrots and yellow sweet potatoes are relatively rich in the substance fat-soluble A, whereas red beets, parsnips, rutabagas, sugar beets, potatoes, mangels and dasheens are very poor in it. Steenbock and Boutwell (2) found yellow maize a sufficiently good source of the fat-soluble A to support approximately the average amount of growth in a male and a female rat when this cereal formed 83 per cent of the diet, and when it was satisfactorily supplemented with respect to inorganic deficiencies. The male appeared rough-coated after the age of eight months. The female produced ten litters of young. The first eight of these all died a few days after birth, but the last two litters were reduced to three and four young, respectively, and were satisfactorily nursed to a state of independence by the mother. White maize, on the other hand, was found without exception to be very deficient in this dietary factor, although several varieties were tested. Animals which derived a large part (85 per cent) of their food from white maize failed to grow beyond a very limited degree and suffered from xerophthalmia and debility of the skin as shown by incrustation of the ears, warts on the nose, infections of the tail and feet, and sores on the body. These

skin conditions are apparently due to lack of resistance of the skin to invasion by an itch mite, although Steenbock and Boutwell make no mention of this. McCollum and Simmonds, in their earlier experience frequently observed these conditions in poorly nourished rats, and microscopic examination of material from the lesions revealed the presence of large numbers of very small mites. In recent years, they have been able to eradicate this parasite from their colony, and the lesions described by Steenbock and Boutwell have entirely disappeared. Such skin conditions are not, therefore, to be regarded as in any way associated with this type of specific starvation.

Red maize, which was free from yellow pigment was likewise found to be free from fat-soluble A, whereas red maize which contained yellow pigment proved a fairly good source of this substance. Variegated maize, in which the pigments were irregularly distributed and which on that account contained red, yellow and blue pigmented portions, as well as some white areas, gave results in feeding experiments which were intermediate between white on the one hand and deeply yellow pigmented varieties on the other. Where yellow kernels occurred mixed with white in variegated ears, a selection of the two kinds showed by appropriate tests that the former contained distinctly more fat-soluble A than the latter.

289. **Certain Leaves Are Very Rich in Fat-Soluble A.**—It was pointed out in 1917 by McCollum, Simmonds and Pitz (3) that the alfalfa leaf is several times richer in fat-soluble A than are such grains as wheat, maize or oat kernel. This line of investigation has been furthered by Osborne and Mendel (4), who have found spinach, alfalfa leaves and clover leaves, to be relatively rich in both fat-soluble A and water-soluble B. Ten per cent of one of these leaves in a diet which derived its sole content of fat-soluble A therefrom, proved an adequate source of this dietary essential for the promotion of fairly rapid growth during periods up to 170 days. Timothy proved somewhat less valuable for this purpose. These results show clearly that these leaves are excellent sources of this vitamin. Cabbage, a thick leaf, specialized as a storage organ, was distinctly poorer in both the uncharacterized essentials under consideration than were thin leaves.

Steenbock and Gross (5) extended these studies and found that 5 per cent of immature alfalfa leaf in the diet as the sole source of the fat-soluble A, the remainder of the diet being

satisfactorily constituted, sufficed to support normal growth, and allowed the rearing of some young. Lettuce, spinach and chard contain fat-soluble A in similar amounts, but lettuce appeared to be somewhat poorer than the other leaves studied. Cabbage was found to be deficient, in comparison with other leaves, in its content of fat-soluble A. These investigators repeatedly emphasized their conviction that the substance fat-soluble A is intimately associated with yellow pigmentation. Those leaves which contained much yellow pigment, although masked by the green pigment chlorophyll, were richer than cabbage, which contains little yellow pigment.

290. **Drummond Suggests That Fat-Soluble A Is One of the Plant Yellow Pigments.**—Among the vegetable foods, therefore, the distribution of fat-soluble A appears to be associated in a remarkable way with yellow pigmentation. The parallelism seemed to Drummond (6) sufficient to warrant an investigation to determine whether this substance might be one of the yellow pigments of plants. He brought rats into a condition in which they were suffering from fat-soluble A deficiency, and then fed them pure and impure preparations of the pigment carotin, which, together with xanthophyll, constitutes the pigments to which are due the yellow color of many vegetable products. The animals did not respond with growth and did not remain free from ophthalmia, as they would have done had a fat containing fat-soluble A been administered. The results indicated, therefore, that carotin is not identical with fat-soluble A.

About the same time Steenbock (7) expressed the belief that the fat-soluble A is one of the yellow plant pigments, although he and Boutwell (8) had earlier stated that this vitamin is not carotin. In several later papers Steenbock has presented data showing the remarkable association of this substance with the yellow pigment of plants. He has shown that when carotin and xanthophyll are separated, fat-soluble A accompanies carotin, whereas the xanthophyll fraction is poor in it.

Drummond and his co-workers have energetically pushed their investigations in the testing of the hypothesis that there is a relation between yellow pigmentation and content of fat-soluble A in food-stuffs. They tested twenty-four different fats and oils which were pigmented to widely differing degrees for their efficiency as sources of this dietary essential, and could discover no relation between vitamin content and color (9).

291. **Stevenson's Observation on Carotin.**—An exceedingly

interesting observation has been recorded by Stevenson (10) working in the laboratory of F. G. Hopkins. She states that an impure preparation of carotin, which did not behave like a source of fat-soluble A when fed as such, acquired the properties of this dietary factor when it was dissolved in palm-kernel oil previously tested and found ineffective for the stimulation of growth. This observation deserves the most careful attention, for if substantiated, it would seem to indicate that fat-soluble A may not be absorbable and utilizable unless it is carried by at least small amounts of fats. She reports also that butter fat can be decolorized of its yellow pigment by absorbing the carotin with charcoal and without impairing in any way its value as a source of fat-soluble A. It will be seen, therefore, that the evidence up to this time is decidedly conflicting on the point as to the relation between yellow pigment and content of fat-soluble A.

Palmer and Kennedy (11) have, however, published an excellent paper on this subject which finally disposes of the question, for they prove conclusively that there is no correlation between the pigmentation of certain foods and their value as a source of fat-soluble A. A brief history of Palmer's studies should precede the discussion. Palmer first took issue with Steenbock on the basis of the former's observation that cottonseed oil, when freed from its resinous substance, possesses a fine golden yellow color and is rich in carotinoids, but does not contain demonstrable amounts of fat-soluble A (12). He also showed that the blood of certain species of animals, as sheep, swine, dog, cat, rabbit, and guinea pig, is free from carotinoids. This would seem, if the vitamin were one of the pigments, to preclude the entrance of the substance into the tissues of these animals. Dolly and Guthrie (13) found adipose tissues and nerve cells of these animals to be free from carotinoid pigments.

292. **Chickens Can Be Reared on Diets Containing No Yellow Pigments.**—Palmer and Kempster (14) succeeded in growing chicks from hatching on a mixture of white maize, white maize meal, white maize bran, skim milk and bone meal. After six weeks the birds began to fail, but responded at once when pork liver was added to their diet. The latter they showed to be free from carotinoids. At three months of age the birds were normal in size for their age. They were then given an occasional feeding of white summer squash and white spanish onions. There was but a trace of carotinoids in the tissues of the birds when grown, as was shown by the lack of pigmenta-

tion of the shanks, ear lobes, beaks and other parts of the body.

At the age of six months the hens began to lay, and seventeen of them produced 893 eggs in 233 days. One hen laid 88 eggs during this period. The yolks were found to be free from carotinoids. A large number of these eggs were incubated. Viable chicks were hatched, which were normal in every respect except for the absence of yellow pigment from the shanks, beaks and other parts. From these results it appears that further attempts to establish a relationship between a yellow pigment and fat-soluble A are futile.

293. **Palmer and Kennedy's Disproof of the Yellow Pigment Theory.**—The investigation of Palmer and Kennedy, referred to above, appears to add the last word to this discussion, and to leave no further room for doubt that the presence of liberal amounts of fat-soluble A in certain yellow pigmented vegetable tissues, and its absence from other varieties of the same species not possessing yellow color, is fortuitous. These investigators succeeded in demonstrating that approximately normal growth and reproduction can be secured in the albino rat on rations free from carotinoid pigments but rich in fat-soluble A.

They first made a critical study of the presence of carotinoid pigments in the albino rat and then instituted growth experiments with this species, using colorless ewe's milk fat as the sole source of fat-soluble A. In other experiments they used, instead of ewe milk fat, colorless egg yolk as a source of this factor. The liver, blood, spleen, suprarenals, adipose tissue, ovary and the fat of milk recovered from the stomachs of very young rats were examined with every precaution for thoroughness to determine the presence of carotinoid pigments. The rat milk was absolutely colorless, as was also the fat separated from the adipose tissue. The fat of the blood, suprarenals, spleen and ovaries, and also the liver tissue of new-born rats was entirely devoid of color. The liver of adult rats fed a diet containing an abundance of plant carotinoids, yielded an oil which was yellowish, but the pigment did not give any of the tests characteristic of carotin. This substance cannot, therefore, be regarded as in any way related to those plant pigments with which fat-soluble A may be concerned.

The milk of the ewe is almost colorless, but gives a very faint test for plant carotinoids. Nine per cent of the diet consisted of this fat, and it was estimated that the ration contained thereof

but 0.127 parts in a million. The diet employed consisted of purified casein, a suitable salt mixture, agar, ewe milk fat, and dextrin carrying the alcoholic extract of ether extracted wheat embryo or germ to serve as a source of water-soluble B. The latter proved an inadequate source of the factor B and was afterwards supplemented by 2 per cent of baker's yeast.

On this diet the rats grew fairly well during two and a half to three months, and three females each produced litters of eleven young. Two of these mothers were able to nurse their litters, which were reduced to six in each case. The young grew in an essentially normal manner. On a similar diet in which 15 per cent of colorless egg yolks served as the sole source of fat-soluble A, six rats grew well, two increasing in weight from about 70 grams to about 230 grams. Two females produced each a litter of young which were normally nourished.

Palmer and Kennedy also pointed out certain numerical relations between the carotin content and fat-soluble A efficiency of various foods. These varied within very wide limits. Thus, 15 per cent of their egg yolks containing no carotin, were at least equivalent as sources of fat-soluble A to 85 per cent of yellow maize, although the latter amount furnished 1,400 parts per million of carotin. Five per cent of ewe milk fat, they estimated to be equivalent as a source of fat-soluble A to 1 per cent of dry spinach. The carotin content of one million parts of rations containing these amounts of materials would amount to 0.073 and 160 parts per million, respectively. The second of these two diets containing about the same amounts of fat-soluble A would contain about twenty-two hundred times as much pigment as the former.

294. **The Stability of Fat-Soluble A Toward Heat.**—In regard to the stability of the fat-soluble A toward heat and reagents, there has existed much difference of opinion. McCollum and Davis (15) observed that egg yolks which had been hard boiled were still a good source of this vitamin, and also that the melting of butter in a hot water funnel and its filtration during one or two hours, followed by solution in ether, filtration and subsequent evaporation of the ether did not appreciably lower the content of fat-soluble A. They, therefore, reported that the substance is fairly stable at high temperatures. In testing their butter fats and egg yolk fats, they employed in their feeding experiments 3 to 5 per cent of one or the other as the sole source of fat-soluble A, and judged from their findings that no extensive destruction could have taken place.

Osborne and Mendel (16) passed live steam through butter fat for two and a half hours, and found that 18 per cent of this fat in a diet served to support normal growth, when there was no other source of fat-soluble A. Since they used such very high fat intake they could have destroyed at least four-fifths of the substance and still had enough left to insure a successful growth experiment. Mendel has recently stated that butter fat heated for many hours to 96° C. would still suffice as a source of fat-soluble A when 0.25 gram per day was included in the diet of the rat. This may be roughly estimated to form about 2.5 per cent of the food mixture. Their data, therefore, support the view that fat-soluble A is a relatively stable substance at high temperatures.

Steenbock, Boutwell and Kent (17) took issue with the statements recorded in the preceding paragraph. They stated: "When butter fat is heated for 4 hours at 100°, so much of its vitamine may be destroyed that with our basal rations, using rats as the experimental animal, no demonstrable amounts of the vitamine remained." Steenbock and Boutwell (18) have, however, recently reported that plant tissues such as yellow maize, chard, carrots, sweet potatoes, and squash, may be autoclaved at fifteen pounds pressure, without causing any noticeable destruction of fat-soluble A.

295. **Fat-Soluble A Is Easily Destroyed by Oxidation.**—Hopkins (19) and also Drummond (20) have shown that oxidation readily destroys the activity of fat-soluble A. It may, therefore, be accepted that the substance is stable toward high temperatures in the absence of oxygen.

296. **Extraction of Fat-Soluble A from Foods by Means of Solvents.**—McCollum, Simmonds and Pitz (21) were the first to study the possibility of extracting the dietary essential fat-soluble A from plant tissues. It was stated, as the result of experiments with several plant oils, that this substance "is not extracted from plants with the fats by such solvents as ether, chloroform, benzene or acetone, and is therefore not found in any fats or oils of plant origin. Hot alcohol does remove it from plant tissues." The solubility of the substance in alcohol was based upon data obtained with the maize kernel. Steenbock and Boutwell (22) later stated "while the vitamine (fat-soluble A) is not extracted from maize by ether, alcohol removes it quantitatively and with little, if any, destruction." Steenbock and Boutwell misrepresented the views of McCollum, Simmonds and Pitz, for after quoting the above statement from their paper

they add: "the reference to its solubility in alcohol (in the paper of McCollum, Simmonds and Pitz) is based on data obtained with the maize kernel which in themselves are not acceptable as McCollum, Simmonds and Pitz were of the opinion that maize generally was very deficient in the fat-soluble vitamine." They referred to an article in the *Journal of Biological Chemistry*, vol. 28, 1916-17, p. 154, in which McCollum, Simmonds and Pitz stated that "the maize kernel contains both the unidentified dietary factors, fat-soluble A and water-soluble B. The former is present in amount too small for the maintenance of growth at the maximum rate in rats, and regardless of how satisfactorily the maize kernel is supplemented in other respects, failure of perfect nutrition will supervene within a few months unless some food-stuff, containing fat-soluble A (butter fat, certain other fats, leaves of plants, etc.) is supplied." In another place McCollum and Davis (23) stated that: "50 per cent of corn added to the fat-free diet is vastly superior to 5 per cent of butter fat (as a source of fat-soluble A) when the animals have been brought to a point near which failure of nutrition would set in." These quotations make clear how little basis Steenbock and Boutwell had for their statement that McCollum and his co-workers had made an unwarranted claim concerning their demonstration of the solubility of fat-soluble A in alcohol, and that they "were of the opinion that maize generally was very deficient in the fat-soluble vitamine."

It has been shown by Osborne and Mendel (24) and by Steenbock and Boutwell (22) that from certain vegetable materials, especially leafy structures, ether or benzene may extract a certain amount of fat-soluble A, whereas water is entirely ineffective.

297. Fat-Soluble A Is Not Destroyed by Saponifying Agents.—In 1914 McCollum and Davis observed that butter fat may be saponified with alcoholic potassium hydroxid and petroleum ether without the destruction of the nutritive principle now designated fat-soluble A or fat-soluble vitamin (25). The soaps resulting from this saponification were dissolved in water and shaken with olive oil. This olive oil had been shown by previous experiments to be ineffective as a substitute for butter fat for the promotion of growth when added to an otherwise complete diet. The olive oil, which had thus been in intimate contact with the soaps of butter fat, was then removed by ether, and the latter evaporated. This olive oil was found by appro-

priate experiments to have acquired the nutritive properties of the butter fat, since it caused a marked response with growth in rats which had been denied the dietary essential fat-soluble A, and whose growth had been for that reason suspended. This experiment showed that the dietary essential in butter fat is sufficiently stable to withstand saponification in nonaqueous solutions. Steenbock, Sell and Buell (26) have since recorded as an original observation their findings that fat-soluble vitamin resists saponification in the cold by alcoholic potash.

The foregoing account of the investigations which have been directed toward discovering methods for the isolation and purification of the dietary essential fat-soluble A, have actually yielded only the information that the substance is thermostable in the absence of oxygen, that it will withstand the action of saponifying agents in the absence of water, and that after saponification it accompanies the carotin fraction of the plant pigments rather than the xanthophyll. We have no knowledge concerning the chemical nature of the substance, and it is to be hoped that the near future will bring important results in the direction of revealing its properties and its chemical composition.

298. **Methods of Estimating the Content of Fat-Soluble A in Natural Food-Stuffs.**—So much interest is shown nowadays in the relative values of different foods as sources of the different vitamins, that students will welcome a brief account of the procedures and their effectiveness as means of determining quantitatively the factor fat-soluble A.

It would seem logical to test the proposition that young animals, restricted to diets, otherwise satisfactory but containing less than the minimum amount of fat-soluble A necessary for the promotion of growth at the optimum rate, would grow at rates proportional to the supply of this dietary essential, the limiting factor. If this were true, it should be possible on a carefully planned diet to judge from the rate of growth in a number of individuals the nutritive value of that diet with respect to this substance. This possibility has been thoroughly tested by McCollum and Simmonds but the results are disappointing. With suboptimal amounts of fat-soluble A, young rats fail to respond in a manner which can be safely used as a basis of accurate comparison of the amounts tested. Nevertheless, rough approximations of the comparative values of different foods for this dietary factor are possible. Osborne and Mendel (4) and Steenbock and his co-workers (5) have reported studies of this nature

which show the great superiority in their content of fat-soluble A of several leafy vegetables over the cereal grains.

A test which has been much used by McCollum and Simmonds (27) is carried out by employing as test animals young rats of the same stock, age and previous nutritive history. They are placed upon a diet which is lacking or essentially lacking in fat-soluble A. A mixture of rolled oats 40.0, gelatin 10.0, a salt mixture 3.7, and dextrin 46.3 per cent, respectively, serves this purpose well. When the initial weights of the animals are about 55 grams, and their ages about 40 days, they usually develop a circular area of puffiness surrounding the eyes in about 30 to 35 days. This sign is premonitory of the onset of ophthalmia, which will now develop within a few days and which is accompanied by excessive secretion in the eyes, and marked edema of the lids. These external signs of ophthalmia are all that need be considered here. Unless the eyes are profoundly damaged recovery takes place on the inclusion in the diet of a suitable amount of fat-soluble A. For the purpose of standardizing conditions with a view to perfecting a quantitative test for this dietary factor they selected, for the addition of the source of fat-soluble A, the time when the puffy ring was easily seen, but when no decided increase in secretion had as yet begun. By comparing the amounts of different food substances given heat or any other treatment tending to destroy the anti-ophthalmic factor necessary to interrupt the course of the disease or to prevent the development of a severe form of ophthalmia, they were able to make fairly satisfactory comparisons of different foods with respect to their curative properties. This method has the advantage of requiring less time and less material than are necessary in a growth experiment. Moreover, the method, they believe, yields results which are more satisfactory. In this method, the animals are brought to the verge of an acute eye disorder, which is averted by an exhibition of a certain quantity of the substance of which their bodies are depleted. The period of observation is shortened to about 6 or 8 weeks.

This method has, however, one element of weakness. A subjective factor is involved in determining the time for beginning the administration of curative measures, but this is reduced to a minimum because of the fairly definite and easily observable incipient edema, and the certainty that once this is seen, the animals will develop severe ophthalmia within a few days.

When small rats are placed on a diet containing traces of the

factor fat-soluble A, there is frequently observed a remarkable variation in the time necessary to bring about ophthalmia. In our experience animals weighing 35 grams suffered from it within 3 to 4 weeks, but in one group of 13, individuals were recorded as showing it after 21, 26, 28, 37, 39 days, respectively, while one showed no signs until the 125th day. Since we have no chemical reaction by means of which fat-soluble A can be detected or estimated, the biological test described appears to be the most satisfactory one available.

299. **Pathological Changes Resulting from Lack of Fat-Soluble A.**—For the purpose of determining the physiological rôle which each of the vitamins plays, it is necessary that we should learn as precisely as possible what happens to the cells composing the different tissues when a break is induced in metabolism through specific starvation for a single one of these, when no other nutritive principle is involved in bringing about metabolic disaster. Research in this direction, which must be achieved through the coöperation of the biochemist and the histologist with knowledge of pathology, may be expected to prove highly fruitful. As yet, however, little effort has been directed to this undertaking. Many attractive chemical problems of a specific nature have held the attention of the chemists in this new field. These could be studied through observing the effects on growth, fertility, nervous symptoms, longevity, or the development of ophthalmia, scurvy or beri-beri. The criteria for the interpretation of the experimental results were such as not to require the services of a pathologist. The pathologist was, however, unable satisfactorily to comprehend the theory underlying the preparation of diets for inducing specific conditions profitable for study, and could not, even if he desired to do so, accomplish anything in this field without the aid of the experienced physiological chemist. With efficient coöperation between specialists in these lines we may confidently expect new and surprising relations to be brought out in future.

Wason (28) has recently studied the pathology of ophthalmia of dietary origin, but was not able to secure any fundamental data concerning the etiology of this condition. She observed in the eyes of rats in which the disease was induced by selective fasting for fat-soluble A, hyalinization or necrosis of the outer layer of corneal epithelium, exudation of serum and cells into epithelium and stroma, and a proliferation of blood vessels and fibroblasts. In advanced cases invariably the anterior and oc-

casionally the posterior chamber were invaded. "The type and virulence of the organisms of secondary infection determine, in part at least, the course of the disease."

Cramer (29) reported an interesting study of the relation of fasting for fat-soluble A to changes in the histological structure in certain adipose tissue, which he designates as "glandular." Several histologists have recognized that adipose tissue in certain parts of the body, especially the subpleural tissue, the neck and interscapular region, the axillæ and around the kidneys, presents a pink and lobulated appearance resembling a fresh pancreas, and differs markedly, therefore, from ordinary adipose tissue and can be recognized macroscopically. This tissue is histogenetically distinct from ordinary adipose tissue. It has been described under a variety of names such as "primitive fat organ," "fat gland," "hibernating gland," "brown fat" and "interscapular fat." This fat has in the embryo a characteristic gland-like structure, and in certain species, as the white rat, domestic mouse and the hibernating animals, retains this structure throughout life. In most species, according to Cramer, soon after birth the tissue acquires the appearance of ordinary adipose tissue.

This "glandular" adipose tissue is very vascular and is distinct from the ordinary form in its function. Many of its cells are polygonal, present a reticulated appearance, and contain numerous small globules of lipins surrounding a nucleus, in contrast to ordinary fat cells which are oval, and generally contain one large fat globule engorging the cell and pushing the nucleus and protoplasm to one side. The "glandular" adipose tissue appears to contain a larger proportion of anisotropic or doubly refracting lipins than ordinary fatty tissue. The cells of the former are much richer in protoplasm than the common type of adipose cells.

During fasting the "glandular" type tends to persist and shows no obvious diminution whereas the ordinary type of adipose tissue is rapidly and greatly diminished. In cretins there are circumscribed swellings of the "glandular" adipose tissue in the neck and axillæ, and there appears to be an hypertrophy of this tissue when the thyroid gland atrophies, suggesting a functional relationship between them. Cramer points out also that there is evidence of such a relation between the "glandular" adipose and the adrenals. There appears to be a particularly close relationship between the lipins of this tissue and those of the adrenal cortex.

When rats are fed a diet of purified food substances, free from all vitamins, this "glandular" tissue loses all its fat and lipins and presents the appearance of a glandular organ. Under the same conditions there is a great reduction of the lipins of the cortex of the adrenals, but this never becomes entirely free from them unless death occurs. Under the influence of such a nutritive disturbance the ordinary adipose tissues lose all their fat and other lipins and revert to the connective tissue type of cells. Cramer suggests that the "glandular" adipose tissue is a reservoir of fat-soluble A, since the disappearance of the characteristic lipins from it and the adrenal cortex is followed by death.

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CHAPTER XIII

THE RELATION OF PELLAGRA TO DIET

300. **Early History of Pellagra.**—Pellagra is a disease of man which is confined to relatively few places. It was discovered in Northern Spain by Casal in 1735 (1), but for many years it was most common in parts of Italy. Aside from Italy and Spain, pellagra has been prevalent during the last century in parts of France, the Balkans, especially Roumania, and for a lesser time in Egypt. It has, still more recently, afflicted many people in the United States. In this country the disease was not recognized with certainty until 1908, but from that year its incidence rapidly increased until by 1917 there were recorded 170,000 cases of pellagra, principally located in the southern states.

301. **Pellagra Symptoms.**—Pellagra is a disease involving the nervous system, the digestive tract and the skin. Usually one of the first symptoms is soreness and inflammation of the mouth followed by the appearance of remarkably symmetrical erythema on parts of the body. The nervous symptoms are more or less pronounced, and become gradually worse as the disease progresses. The spinal cord is especially the seat of injury, but the central nervous system is also involved in many instances.

302. **Theories as to its Cause.**—Several views have been proposed to explain the etiology of this disease. Marzari, more than a century ago expressed the belief that pellagra resulted from the excessive use of maize as food. Italian investigators later accepted the view that it was caused by eating mouldy maize, the symptoms being caused by a toxic substance produced during the spoilage of the grain. Two other theories have been advanced to account for its etiology: one that it is caused by an infecting organism, and the other that it is in some way related to faulty diet. None of these views have been established by entirely satisfactory evidence, but the data now point incontrovertibly to a relation between the diet and pellagra. One group of investigators believes that pellagra is an infectious disease, but admits that lowered vitality from faulty nutrition is a

very important predisposing factor. Another group holds that the syndrome results from the lack in the diet of a specific protective substance, and that it is, therefore, analogous to beri-beri and scurvy. Since almost all students of this disease are now agreed that there is some relation between the character of the diet and susceptibility to it, the present chapter will be limited to a discussion of the evidence of the rôle of nutrition as an etiological factor in pellagra. Roussel (2) as early as 1845 stated that the most effective treatment of pellagra is a milk diet. Lussana and Frua (3) in 1856 studied the effect of improvement of the diet of pellagrins, and reported that they reduced the mortality in about 8,000 cases, from 24.5 to 4.5 per cent, and that they increased the rate of recovery from 20 to 70 per cent. The idea that the disease could be prevented or cured by proper diet dates back many years.

In 1909 the American investigators Wussow and Grindley (4) emphasized the fact that the diet of the insane patients under their observation was mostly composed of vegetable products, and that it had an especially low content in animal protein. In the light of what has been said in earlier chapters about the specific dietary properties of the different kinds of vegetable and animal food-stuffs, which can be, to a truly remarkable extent, correlated with their biological function, we are able to appreciate the fact that a fairly satisfactory diet can be prepared from vegetable foods supplemented with small amounts of products of animal origin provided the selection of the articles which enter into the diet be a fortunate one. At the time of the investigations referred to, however, the significance of the proper selection of food for the promotion of well-being was not at all appreciated.

303. **Goldberger's Studies on the Relation of the Diet to Pellagra.**—In 1914 Goldberger (5) began an investigation of the factors operating in the etiology of pellagra. His studies have proven of the greatest significance in clearing up this problem. He noted the fact that in several institutions where pellagra was either epidemic or endemic among the inmates, the physicians, nurses and attendants were almost without exception immune to the disease. This indicated that contact with persons suffering from pellagra, or opportunity for transmission by bedbugs, with which such institutions are almost always infested, did not seem a satisfactory explanation for the transmission of the disease. In institutions where the food purchases were assumed

to be alike for patients and attendants, it was pointed out by Goldberger, that the diets of the two groups were not comparable. The nurses and attendants, due to their favorable position, chose the best articles, and diverted certain foods to their own table where the amounts did not suffice for all. The patients were thus placed at a disadvantage in regard to the quality of their food. Thus where the meat and milk purchased for an insane asylum was inadequate, the tendency would be for the milk and the desirable cuts of meat to find their way to the table of the attendants, while the unattractive pieces of fat or gristle would be served to the patients. Physicians, nurses and attendants were also in a position to supplement the institutional diet in any manner they saw fit.

Goldberger gained the impression after an examination of the character of the dietaries of certain institutions where pellagra was of common occurrence, that more cereals and vegetables were used than in the dietaries of people in better financial circumstances who were practically immune to the disease. This led him to undertake a study of the possibility of preventing the disease in institutions by improving the dietary.

At that time nothing was understood of the peculiar nutritive properties of the different natural food-stuffs. These have become known through the systematic studies of individual foods by means of the biological method introduced in 1915 by McCollum and Davis (6). Goldberger could therefore do nothing better than to conclude that by comparing the diets of persons who developed pellagra, with those of people living in the same region but remaining free from the disease, he could arrive at a conclusion as to the kind of modification of the former type which should be necessary to test the relation of the diet to the incidence of pellagra. It was apparent to him that the habitants who remained free from the disease, took a diet which contained much greater quantities of fresh meats, eggs and milk, than those among whom the incidence was high. The well-to-do part of the population maintained a distinctly better dietary throughout the year than did the poorer people, who with the seasons suffered much greater changes in their food supply. The winter diet of the latter would naturally be simpler and more monotonous than one which would be available for a moderate expenditure of money during the summer months. The recognition of the importance of seasonal variations in the diet as an etiological factor in pellagra was one of great importance. It is true, how-

ever, that while pellagra is in great measure confined to the poorer classes, and afflicts those who live in the less desirable parts of cities and villages, this is by no means always the case, for it occurs among the well-to-do, but much less commonly than among those who depend upon a daily wage. As will be seen later, this can best be accounted for as due to idiosyncrasies which lead the patients to make a faulty selection of foods.

304. **The Investigations of the Robert M. Thompson Commission, and the Thompson-McFadden Commission.**—In 1913 the Thompson-McFadden Commission, consisting of J. F. Siler of the U. S. Army; P. E. Garrison of the U. S. Navy, and W. J. MacNeal of the New York Post Graduate Medical School, began an extensive epidemiological study of pellagra in Spartanburg County, S. C. They collected a large amount of data regarding the nature of the diets of pellagrins. The information was obtained from statements of physicians, patients, storekeepers, millers, neighbors and others.

In their first years of study no satisfactory data was secured relating to the diets of the non-pellagrous portion of the population, but the tentative conclusion of the Commission was that their observations upon the habitual use of the more common food-stuffs, failed to disclose any points of difference between the pellagrous and non-pellagrous portions of the population. Their investigations in succeeding years, which were extended to include an examination of the dietaries of non-pellagrins tended to confirm their belief that there is no relation between the character of the diet and the incidence of the disease (7).

Goldberger has pointed out (8) that data relating to diet to be of value in such epidemiological studies, must be secured with individuals, either pellagrins or non-pellagrins, and not be of a general nature, applying merely to the family group. It must be kept in mind that the changes in the diet with the seasons may be of the greatest importance. He also pointed out that the condition which it is necessary for the subject to reach before a diagnosis of pellagra would be made, should be carefully stated. Much of the conflicting data and resulting conflict of views based on the study of experimental data can be explained through failure of investigators to appreciate these facts. It is in part due to the full appreciation of these points by Goldberger, which gives his studies a superior value.

The Thompson-McFadden Commission came to the conclusion as the result of several years of observation that "pellagra spread

from a preëxisting case as a center in the six villages studied," and that "pellagra morbidity was higher in congested communities using surface privies than in more sparsely settled districts in which similar methods for the disposal of excreta were employed." Further, ". . . the endemic foci of pellagra were located in the districts in which surface privies were in use." In two cotton mill villages completely equipped with a water-carriage system of sewage disposal it was impossible to find cases of pellagra which had certainly originated there, although some cases which had originated elsewhere were present. It was decided that the stable fly (Stomoxys calcitrans) displayed certain salient characteristics which seemed to qualify it for the rôle of a transmitter of pellagra (9).

305. **The Studies of Jobling and Peterson on Pellagra in Nashville.**—Jobling and Peterson (10) arrived from their studies of the disease in Nashville at a similar conclusion as to the transmissibility of pellagra. They were led by their observations to conclude that the disease attacked those who were domiciled in parts of the city which were either without sewage disposal or where it was inadequate. Pellagra could be correlated with unscreened houses, and access of flies to human excreta and to human habitations.

With regard to diet, they stated that the inhabitants of the South consume excessive amounts of carbohydrates and fats, but pointed out that in Nashville the people of the class in which pellagra occurred most frequently, eat during the spring and summer, a great deal of potatoes, fruits and other fresh foods. This led them to the belief that pellagra cannot be due to a deficiency of a "vitamin" in the sense that beri-beri is. They stated in this connection: "It seems strange, if this theory is correct, that pellagra should be so rare in winter when green foods are scarce, and so frequent in the spring and summer when green foods and fruits are plentiful and cheap." Goldberger felt that this very fact that the scarcity of fresh fruits and vegetables, especially green foods, in winter, was significant as an argument in favor of the hypothesis that the disease was the result of a faulty diet. It is reasonable to suppose that any effect on health which might follow the adherence to a faulty diet, would, under such circumstances, appear at the end of winter, and the effect of a more satisfactory diet in spring and summer would not necessarily become apparent for a time in persons who had been seriously injured by several months re-

striction to a faulty diet. It may require several months to induce scurvy or beri-beri in man through the agency of a defective diet, and recovery is slow, even when the diet is modified so as to contain everything which is physiologically essential.

306. **The Eradication of Pellagra from Institutions by Modification of the Diet.**—Goldberger, Waring and Willett (11), in 1915, studied the conditions which might explain the differences in the incidence of pellagra in two groups of children in an orphanage at Jackson, Miss. In this institution there were children from infancy to twelve years of age. The presence of pellagra was practically confined to the group between the ages of six and twelve years. This was correlated with differences in the diets of the two groups with respect to the content of fresh meat "and other animal protein," the older group being denied these special articles of diet. Analogous conditions were discovered at other institutions.

It was the suggestion gained from earlier studies on beri-beri which led Goldberger and his co-workers to reason from analogy that pellagra was in some way either prevented or cured by some specific substance or substances contained in fresh protein foods. With this idea in mind they instituted an experiment to test whether pellagra could be prevented or cured by a proper diet. The experiment was carried out at two orphanages and an insane asylum. It was not possible at that time to interpret as satisfactorily as can now be done, the nature of the faults in a diet. Goldberger could, therefore, do no better than to add to the institutional diets liberal amounts of each of the more important articles such as fresh meat, eggs and milk, and fresh vegetables, since the institutional diets differed from the better class American diets in the absence of these foods.

In one of the two orphanages under observation during 1914, there was no recurrence of pellagra in any of the 67 persons afflicted, who were under surveillance at least until the anniversary of their attack. Among 99 pellagrin residents of this institution who were under observation for at least a year there was not a single case of the disease after the change in the diet of the institution. At the other orphanage 105 pellagrins were observed for at least a year, including the anniversary of their attack, and there was not a single case of recurrence. Sixty-nine individuals who had not suffered from the disease were observed for at least a year and among these not a single case developed.

At the Georgia State Asylum, which was an endemic focus of pellagra, the diet of two wards was modified so as to greatly improve it, but no change was made in hygienic or sanitary conditions. In these two wards 72 patients suffering from pellagra during 1914 were kept under observation at least beyond the anniversary of their last attack, but not one of them showed any sign of recurrence. During the corresponding period 47 per cent of 32 control patients in another ward showed definite recurrences. The conclusion drawn by Goldberger and his associates was that pellagra can be prevented by an appropriate diet, even when the hygienic conditions are unfavorable.

307. **An Attempt to Produce Pellagra Experimentally in Man by Faulty Diet.**—Having convinced himself that pellagra could be prevented by a suitable dietary, Goldberger planned an experiment to determine whether a faulty diet of the type common among pellagrins would produce the disease in man. The plan involved restricting men to a diet similar to those which had been supplied to the institutions where pellagra had been endemic, and where it had been relieved by the changes in the food supply described above. This was, indeed, the type of diet characteristic of the homes of the cotton mill workers throughout the section of the South where pellagra was very common. This experiment is of extraordinary interest because of the care with which it was planned and executed, and because of the unquestioned skill of the observers.

The Governor of Mississippi was induced to offer pardon to any of the healthy white men in the state prison who would submit themselves as subjects of experiment. Twelve men offered themselves and of this group eleven actually underwent the test. White, male adults were selected because this group of the population in pellagrous districts had shown a lower incidence of the disease than any other race, sex or age. It was believed that the experiment, if it was successful in inducing pellagra in these men, would be the more conclusive because carried out with this selected group of subjects.

The fact that attacks of pellagra occur most frequently in the spring and early summer, was also taken into account, and the experiment was started at a season of the year when, if pellagra was successfully produced after a period corresponding approximately to the winter season, during which the people of the South restrict themselves to a simple and monotonous diet, the disease would appear out of season, i. e., in the autumn.

The men were placed on the experimental diet on April 19, 1915, and continued with it until October 31st of the same year.

The experiment was carried out on the Rankin farm of the Mississippi penitentiary. On this farm were a considerable number of convicts who were regarded as sufficiently trustworthy to be permitted to work on the farm in some capacity. These men were under observation as controls. The time during which these men were observed varied greatly, but eight were observed for periods of eight to nine months. Of one hundred and eight convicts on the farm at the beginning of the experiment, thirty were present until it was terminated. No case of pellagra occurred on the farm during the experiment, or had been noted among the convicts or attendants at the institution in previous years, although it was fairly prevalent in the country surrounding. There would seem to be no question of the fact that the eleven experimental subjects were entirely protected against exposure to pellagra, for they were under guard throughout the experiment.

The diet of the men in the experimental group consisted of white wheat flour, degerminated corn meal (maize), polished rice, starch, sugar, molasses, pork fat, sweet potatoes, collards, turnip greens and coffee. From the data furnished by Dr. Goldberger, I calculated that less than 4 per cent of the total energy value of the diet was derived from cabbage, collards, turnip greens and sweet potatoes. The diet was, therefore, essentially derived from degerminated cereals, and products made from these, together with molasses and fat pork. It will be recalled that it has been thoroughly demonstrated that such a diet is not adequate for the maintenance of health in an adult for a very long period. The average protein intake was 41-54 grams; of fat, 91-134 grams, and of carbohydrates, between 387 and 513 grams per man per day (12).

At the end of five and a half months six of the eleven men were diagnosed as showing the skin lesions characteristic of incipient pellagra. The diagnosis was concurred in by a number of dermatologists who were familiar with pellagra. The first evidence of skin eruption was seen on all the men who became affected, as a bilaterally symmetrical scrotal eruption. Erythema appeared on the backs of the hands of two of the men, and gastro-intestinal and nervous symptoms were noted in all. Goldberger and Wheeler (12) hold the view that it is probable that the first appearance of skin lesions in their experi-

mental men on the scrotum, is to be looked upon as the result of some peculiarity in the diet employed. They regard it as probable that the several clinical manifestations of pellagra, such as the appearance of the initial lesions on the back of the hands, or back of the feet, as due to specific peculiarities in the diet which brought on the pathological state. Thus they suggest that, although their group of subjects was served the same diet, they did not all eat the same proportions of different foods. Some traded dishes, and so one may have eaten more green leafy foods; another more sweet potatoes, etc. On this basis they would account for the fact that one man lost much weight during the experiment (124 to 99.5 lbs.), whereas another lost much less (126-118 lbs.), during the same interval. The idea that there is in such a condition as pellagra an intimate relationship among the several components which go to make up the diet, and the specific clinical manifestations which the disease may assume, involves a degree of specificity in the effects of faulty diet, which has as yet scarcely been acknowledged by investigators.

308. **Attempts to Produce the Syndrome of Pellagra in Animals.**—Attempts to produce the syndrome of pellagra in animals by confinement to faulty diets have not been wanting. Chittenden and Underhill (13) fed dogs, exclusively on vegetable foods, and observed that they did not thrive. One diet, consisting of crackers (bolted wheat flour), peas and cotton-seed oil, produced in dogs restricted to it for several months, a condition regarded by these investigators as strikingly suggestive of pellagra in man. The animals developed inflammation of the mouth with sloughing of the mucosa, diarrhea, and skin changes of a nature regarded as analogous to those seen in pellagra.

McCollum and his co-workers had by this time applied the biological method for the analysis of a food-stuff to all the more important cereals and legume seeds. Their results showed that a diet of peas, wheat flour and cotton-seed oil such as Chittenden and Underhill had employed, could be supplemented with purified protein, mineral salts and fat-soluble A, so as to be made adequate for the maintenance of growth and health in the rat. After the appearance of the paper of Chittenden and Underhill, McCollum, Simmonds and Parsons (14) tested this theory by feeding the diet of Chittenden and Underhill supplemented with purified food-stuffs in various ways to young rats. The results justified the prediction that these three types of corrections

were all that was necessary to make the diet complete, for the rat. From these results they drew the conclusion that the diet used by Goldberger and his associates could not possibly be deficient in any unidentified dietary essential analogous to the anti-neuritic or anti-scorbutic substances. At that time there was not available as there is to-day a demonstration of the fact that one species of animal may have decidedly different nutritive requirements than another, with respect to at least one of these dietary factors. The classic example of this is seen in the rat which does not require the anti-scorbutic substance, and which is incapable of developing scurvy, whereas the guinea pig is very susceptible to this disease. It no longer seems warranted to assume that because the rat does not suffer injury from confinement to a certain diet, that this is sufficient evidence that the diet is complete for another species. The possibility remains that man may require a substance for protection against pellagra, which the rat is able to synthesize or to dispense with. Further investigations are required to settle this question.

McCollum, Simmonds and Parsons (14) were inclined to interpret their results as supporting the view that pellagra is an infectious disease, and that the rôle of diet in its etiology involves only increased susceptibility to infection due to lowered resistance caused by faulty diet persisted in during the winter months by many people in the South. Their results supported incontrovertibly the contention of Goldberger, that the type of diet which he fed to the prison squad was incomplete, and would lead to steady loss of vitality, and they made clear the exact nature of the deficiencies of the prison dietary in so far as they relate to the nutrition of the rat.

309. **Attempts to Transmit Pellagra to Healthy Subjects.**—Goldberger and fifteen of his associates next tried in a number of ways to transmit pellagra to themselves by a series of innoculations with blood, nasopharyngeal secretions, feces, urine and desquamating epithelium. The results of this heroic experiment were entirely negative. Not a single one of the volunteers showed any evidence of the disease. These subjects were all presumably nourished on a satisfactory diet previous to and during the experiment, and this could be interpreted as evidence in support of the view that pellagra is a disease of low virulence, and that it is liable to attack only that portion of the population which, for one reason or another, has suffered a lowering of resistance (15).

310. **The Maize Theory of Pellagra Brought up Again.**—The Director of Medical Services of the Egyptian Expeditionary Force directed that a committee of medical men in the British Army make a study of the prevalence of pellagra among Turkish prisoners of war (16). This report was made by Boyd and Lelean, who concluded that the maximum distribution of pellagra appeared to correspond geographically to the broad belts where maize grew best, and hence formed the larger proportion of food in the classes most pellagrous. They attributed pellagra to starvation for protein, especially to a low intake of protein of low biological value. It was believed that on this theory the frequent occurrence of pellagra among those who ate mouldy maize could be explained by a lower utilization of the proteins of spoiled grain than of unspoiled. The occurrence of pellagra among those who had never eaten maize could be explained as a consequence of their securing through some dietetic error a protein supply of low biological value.

311. **Voegtlin's Treatment of Pellagra with Vitamin Preparations.**—Voegtlin (17) has recently described experiments in the treatment of pellagra, which seem to fall little if any short of a demonstration that pellagra is a deficiency disease in the same sense as beri-beri or scurvy. This investigator has been one of the most careful students of the etiology of the disease. In 1914 (18) he made the first attempt to interpret the nature of the deficiencies of the diets which are common among those classes of people of the United States among whom pellagra is of frequent occurrence. He proposed (1) a deficiency or absence of certain "vitamins"; (2) the presence of some toxic substances; (3) a deficiency in certain amino-acids. Later researches, especially those of McCollum and Simmonds have shown that the articles which entered into the diet used by Goldberger, cannot contain sufficient amounts of toxic substances to account for the ill-effects observed when animals are restricted to them singly or collectively. Concerning the other two proposed explanations for pellagra, both are still debatable contributing factors.

In 1914 Voegtlin tested on over one hundred patients in the pellagra hospital at Spartanburg, the effects of two types of diets on the clinical condition of the disease (18). Patients with a moderate attack of pellagra uncomplicated by any other disease, were placed upon a diet which closely resembled that which they were accustomed to before the attack. These will be desig-

nated as diets X and Y. Diet X consisted of the following ingredients:

Wheat bread	300 grams.	
Butter	30 "	
Cabbage	100 "	
Corn meal (maize)	50 "	
Ham	25 "	
Hominy	75 "	This diet contained 50.5 grams of protein; 89.8 grams of fat; 350.8 grams of carbohydrate, and yielded 2473 calories of energy.
Corn syrup	75 "	
Pork	50 "	
Potatoes	150 "	
Prunes	30 "	
Turnip tops	100 "	
Sugar	40 "	
Milk	40 "	

Of the effect of restricting pellagra patients to this diet Voegtlin says: "Almost without exception the general clinical condition of these patients remained either stationary or gradually became more aggravated simultaneously with an increase in the pellagrous manifestations. The skin lesions often spread to parts of the body which had not been affected previously; there was also an increase in the stomatitis and the gastro-intestinal symptoms. The appetite, as a rule, was good for the first few weeks, but diminished gradually. The nervous manifestations, such as disturbances in sensation, reflexes, and mentality either showed no change or increased in severity. A few cases developed an acute psychosis. A careful examination of the dietary record showed that the patients had consumed sufficient food." The patients were changed after a time to diet Y, the composition of which was given as follows:

Wheat bread	300 grams.	
Butter	45 "	
Corn meal	50 "	
Eggs	100 "	This diet contained 102.9 grams of protein; 115.3 grams of fat; 316.2 grams of carbohydrates, and furnished 2781 calories of energy.
Meat	100 "	
Orange juice	100 "	
Potatoes	150 "	
Prunes	30 "	
Sugar	40 "	
Milk	1000 "	

On diet Y, which differed from diet X in containing 4 eggs, 100 grams of fresh beef and one liter of milk (somewhat more than one quart), the patients showed gradual improvement, ending in many cases in the complete disappearance of all recognizable

manifestations of the disease. Another group of patients which was placed on diet Y immediately upon their admission to the hospital, showed definite improvement within two weeks. Within two months the patients were judged to have recovered from the disease, except in a relatively few cases in which it was far advanced. Some of these did not show any benefit from the improved dietary.

Voegtlin next placed patients on diet X for a time until it was observed that their clinical condition remained stationary or grew gradually worse. Some were then given one of the following extracts of natural food-stuffs:

(1) A fat-free, alcoholic extract of yeast or rice polishings.
(2) A fat-free alcoholic extract of ox liver or thymus gland.

The first of these extracts was chosen because it contained a great abundance of the anti-beri-beri substance, water-soluble B. The second contained a relative abundance of fat-soluble A and water-soluble B. The results indicated that the administration of extracts of yeast or rice polishings did not modify the course of the disease in patients maintained on diet X, with the possible exception of one case in which certain well-marked nervous symptoms disappeared coincident with the treatment. Voegtlin states that "the administration of the liver preparation to pellagrins was followed by an improvement in their condition, apparently comparable to that produced by the consumption of a diet containing a considerable amount of milk, eggs and meat. The evidence so far available, therefore, indicates that the dietary defect presumably responsible for pellagra is distinctly different from, and probably more complex than the one causing human beri-beri."

If these results are confirmed by further experiments it is difficult to see any other interpretation which can be placed upon them than that pellagra is a specific deficiency disease, due to the lack of some substance or substances which are not abundant in the articles which entered into the composition of diet X, but were more abundant in milk, eggs and meat, at least in liver. Voegtlin does not imply that pellagra is necessarily due to a deficiency of the diet in a specific substance such as a hypothetical pellagra "vitamin," proposed by Funk. He holds rather that the pellagrous syndrome is caused by a *combination of the deficiencies in some of the well-recognized food factors.*

312. **Voegtlin's Results Indicate Vitamin Deficiency.**—I am unable to see the logic of Voegtlin's reasoning. An alcoholic extract of liver would not modify the inorganic content of diet X, nor the biological value of its proteins. The content of diet X in the anti-neuritic, anti-scorbutic and fat-soluble A factors, when compared with ordinary standards, would seem to be moderately satisfactory. Poor quality of protein and relative shortage of the anti-scorbutic substance were the two deficiencies which anyone familiar with modern nutrition studies would suggest on inspecting the formula of this diet. The extract of liver would contain an abundance of two at least unidentified dietary factors, but would not improve the diet in respect to the two known deficiencies. For the rat, at least, it is certain that diet X would be supplemented by the addition of purified protein and mineral salts, so as to be entirely adequate for nutrition of young animals during growth, and for the maintenance during many months of fairly good vigor in the adult. For this species, therefore, there is no necessity for postulating the need of a supplementary addition of a hypothetical anti-pellagra substance. It seems that if liver extracts are found so effective in supplementing the diet on which the condition of patients remained stationary, or grew worse, the explanation to which one must be tentatively driven is that Funk's hypothesis that pellagra is actually a specific deficiency disease must be correct. Certain it is, however, that Voegtlin is illogical in trying to hold simultaneously to two views, viz.: that there is something in an alcoholic extract of fat-free liver which cures pellagra, when it is made to supplement diet X, and that the syndrome is caused by a combination of the deficiencies in some of the well-recognized food factors.

In the preparation of the liver and thymus extracts Voegtlin and his co-workers extracted the dried glands with alcohol at room temperature, and after filtration a considerable part of the alcohol was evaporated at 35°-40° C. in vacuo. The viscous substance remaining was extracted twice with ether in a separatory funnel. Three layers formed: an upper layer consisting of ether containing fats and lipins; a middle layer consisting of white or yellowish insoluble residue, and a lower layer consisting of a mixture of substances of oil-like properties. The last-named layer was designated as the "vitamin fraction." In the treatment of adult pellagra patients, daily doses of this oily material equivalent to one kilogram of fresh liver or thymus were administered.

313. **Occurrence of Pellagra in Nursing Infants.**—Voegtlin and Harries (19) have reported a number of cases of pellagra in infants which were nursed by pellagrous mothers, and cite older literature which shows that in the past a considerable number of cases of pellagra have been observed in infants. The cases observed by Voegtlin and Harries were observed in the light of all the accumulated knowledge of recent years concerning the relation of the disease to faulty diet, and are therefore of special importance in revealing the cause of this condition.

314. **Report of Cases of Pellagrous Mothers Nursing Babies Who Did Not Develop the Disease.**—A mother suffering from severe pellagrous lesions was admitted to the hospital while nursing a seven-months-old infant. The child did not show any symptoms of the disease. The mother was placed upon the following diet (Diet A) during her stay of 35 days in the institution. This diet is of a type commonly used by pellagrins.

DIET A.

Breakfast.—Hominy, 75 grams; butter, 15 grams; corn syrup, 30 grams; wheat bread, 100 grams; coffee, with 20 grams of sugar and 20 c.c. of milk.

Dinner.—Potatoes, 150 grams; cabbage, 50 grams; turnip tops, 50 grams; fat pork, 30 grams; wheat bread, 100 grams.

Supper.—Corn meal mush, fried in pork fat, 50 grams; lean boiled ham, 25 grams; prunes, 30 grams; wheat bread, 100 grams; coffee, with 20 grams of sugar and 20 c.c. of milk.

Samples of milk were secured from this patient, and from four others who were restricted to the same diet. These were analysed by the most approved chemical methods for all constituents which can be determined by such methods. The lactose, fat, total nitrogen and total solids were found to fall within normal limits, but were below the average in amounts. The total ash and phosphorus content were normal, but the sodium and chlorin content were above the normal, whereas the calcium, magnesium and potassium were present in amounts below the normal. No tests were applied to show the vitamin content of any of these milks. Their total volume was found to be greatly diminished in many cases.

None of the infants of five mothers suffering from somewhat severe symptoms of pellagra, showed any signs of the disease. It is very difficult to in any way correlate the occurrence of pellagra in infants with the character of the milk of mothers who

nurse them, for it would seem that if any relation existed between the character of the diet of a mother and the causation of her attack, the infants suckled by them should, especially when the symptoms are severe, more frequently develop pellagra. On the contrary, pellagra in infants which are nursed by mothers suffering from the disease is by no means common. Such mothers usually feed their infants on the same food which they themselves eat, when the breast milk is too scanty to suffice for the children. This replacement of a considerable amount of mother's milk by food which leads to pellagra in the adult should, theoretically, go far toward causing the disease in an infant, yet this result is seldom observed. No one has been able to demonstrate the presence of anything toxic in the milk or blood of pellagrins, so the theory that the disease may be an intoxication has no support.

There can be no reasonable doubt that the milk produced by pellagrous women, is in general deficient in all three of the vitamins which are known to produce specific syndromes, and the occasional occurrence of pellagra in infants where the mothers are suffering from this disease, could, on first thought, seem best accounted for on the assumption that it is caused by lack of a specific vitamin. This view receives support from the experimental work of Voegtlin reported above, in which pellagrins were reported to have been greatly improved by "vitamin preparations" made from liver or thymus. It would seem logical that the mother might, even when she were so severely starving for a hypothetical anti-pellagra vitamin, as to cause in her a severe form of the disease, still continue to transfer to her milk such small amounts of the substance in question as might be furnished in her food, or be available from her own tissues. This idea is not supported by analogy with the character of the milk produced by lactating females whose diets are lacking in one or another of the factors, A, B or C, since these are not in the milk unless supplied by the diet of the lactating mother.

The last suggested hypothesis, that when the mother has pellagra but her nursing infant does not, protection is afforded the latter through sacrifice on the part of the mother for the teleological purpose of preserving her offspring, receives a severe blow by the observation of Voegtlin and Harries. They observed an infant about one year of age, to develop severe symptoms which unmistakably indicated pellagra, although her mother,

nursed her throughout this time, and showed no evidence of the disease. She was, however, obviously undernourished and suffered from chronic indigestion. No other member of the family consisting of parents and four children besides the patient, showed any signs of pellagra. This observation would seem to entirely negate the theory that the disease can be explained as being due to lack of a specific vitamin in the mother's milk, for she did not have the disease. This particular case would seem to support the view that pellagra is due to an infection with which this child came into contact.

315. **Vedder's Interpretation of Existing Data Relating to the Cause of Pellagra.**—Vedder (20) has brought together a number of salient facts derived from the observations of several students of pellagra, and interprets them as showing that "there is a certain similarity between pellagra and other known deficiency diseases, namely, beri-beri and scurvy," and "much of the evidence that has been presented as a proof of the infectious nature of pellagra can be reasonably explained in accordance with a deficiency hypothesis." He further concludes: "A deficiency is demonstrable in the diets of most pellagrins. This deficiency appears to me to result from the too exclusive use of wheat flour, in association with corn-meal, salt meats and canned goods, foods that are known to be deficient in vitamins."

Vedder has brought out some very important points. "The gastro-intestinal lesions in pellagra and scurvy are analogous." Diarrhea, enteritis, ulceration of the intestines and hemorrhage into the mucous membranes are observed in both conditions. "There are similar nervous symptoms in pellagra and scurvy." Osler (21) states that scurvy is to be differentiated from pellagra.

Suggestive similarities exist between pellagra and beri-beri. The mucous membranes of the stomach and duodenum may be swollen and inflamed, and may present ecchymoses and erosions. "Similarities in the lesions in the nervous system and in the symptomatology referable to the nervous system in pellagra and beri-beri can be distinguished. The pathologic alterations that occur in the cord in pellagra are profound and striking." It has been repeatedly demonstrated that in beri-beri there is degeneration of many of the motor cells in the cord. Roberts (22) describes the extensive degenerations which have been observed in the spinal cord in pellagra. Vedder states "Now, if we compare this picture (20) with the changes found in the cord in beri-beri, we find that beri-beri is characterized by the same

scattered degeneration of the fibers and similar changes in the cells of the cord."

Vedder points out that central neuritic symptoms are very common in pellagrins, and that exactly such changes in the nervous system caused beri-beri for many years to be regarded as an intoxication. "The fact that the spinal fluid in pellagra is normal, points toward deficiency, since it seems improbable that such extensive changes in the spinal cord could occur as the result of an infection without producing the corresponding changes in the spinal fluid. Even the skin lesions which are so characteristic of pellagra may be referable to changes in the cord. Otherwise, how can we explain the marvellous symmetry that is practically the constant characteristic of this symptom?" These are certainly very pertinent questions to raise in connection with any decision as to the nature of the factors involved in the etiology of pellagra.

It is evident from the discussion presented above of the conflicting evidence which is presented in the extensive literature relating to pellagra, that it is not at present possible to give credence to all the data which appear to emanate from reliable sources, and to be derived from observations which seem to be accurate, and formulate any satisfactory theory concerning its etiology. Epidemiological, clinical and chemical methods have alike failed to establish beyond question the cause of the disease.

316. Pellagra Can Be Prevented by a Satisfactory Dietary Regimen.—From the standpoint of prevention, the researches in this field have, however, been of the greatest importance. It is abundantly established that pellagra is in some manner caused by faulty diet, and that the type of diet which is concerned in its etiology is one derived largely from milled cereals, tubers, molasses, syrup and fat pork (23). It is absolutely proven in numerous cases, that milk is the most effective therapeutic agent, and that the inclusion of a liberal amount of milk, together with meats, eggs and leafy vegetables in the diet will prevent the disease. All authorities are agreed that there is but one effective method of prevention or of treatment for pellagra, viz., a satisfactorily constituted diet.

Pellagra afflicts the people of the South, largely because they are engaged in the cultivation of a cash crop (cotton), or in its manufacture. Under such conditions the food supply is derived in great measure throughout the year from the grocery store, and during the winter season, practically exclusively so.

The grocer, in modern civilized and progressive communities, has come in recent times, to restrict his line of foods in great measure to milled cereals and canned goods which are derived either from muscle meats or from seed products (beans, peas, corn, etc) and molasses. As has been repeatedly shown by experiments on animals, it is not possible to prepare from such a list of foods a diet which will promote well-being over any prolonged period. On such a diet ill health and inefficiency are to be expected, and experience has abundantly shown that this result is being realized where such dietary practices prevail.

The knowledge of the methods by means of which pellagra can be eradicated is, therefore, quite adequate, and as soon as it can be applied practically where needed, the disease may confidently be expected to disappear in proportion to the extent to which reform in the diet of the population can be brought about. The reduction of the consumption of milled cereal products, molasses and fats, and a substitution of liberal amounts of the protective foods, milk and the leafy vegetables will free any community from this scourge, which is now (1921) reported to afflict more than two hundred thousand people in the United States.

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FIG. 13.—This picture illustrates the emaciated appearance of a middle aged rat after being fed about four months on a diet consisting of bolted flour, degerminated corn meal, rice, sugar, starch, pork fat, molasses, sweet potato, and cabbage. Such a diet has been reported by Goldberger to have produced pellagra in man in five and a half months. This diet affords wide variety and consists of wholesome food products, yet fails to maintain normal nutrition because it contains too little of the *protective foods*, milk, eggs and the leafy vegetables.

FIG. 14.—Illustrates the remarkable bilateral symmetry of the skin lesions of pellagra.—Courtesy of the Thompson Pellagra Commission.

FIG. 15.—Illustrates the skin lesions on the arm and hand of a pellagrin.—Courtesy of the Thompson Pellagra Commission.

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CHAPTER XIV

THE RELATION OF THE DIET TO THE ETIOLOGY OF RICKETS AND RELATED CONDITIONS

317. **The Prevalence of Rickets in Children.**—There are probably no conditions which contribute more to physical inferiority in man than defects in skeletal development. Most important among these is the result of a syndrome designated as rickets. This disease varies in severity, and individual cases present, therefore, pictures which differ in some details, but all cases have certain characteristics in common. Rickets leads to deformity, due to abnormal enlargement of the ends of the bones, and to distortion due to bending owing to lack of resistance of the bones to the body weight, to muscular tension and to atmospheric pressure. The latter factor is especially important in changing the form of the thorax. Bow legs, knock knees, enlarged joints, flat or deformed chest and abnormal conformation of the skull, are the result of the failure of the bones to develop in a normal manner.

Rickets is essentially a disease of infancy and early childhood, although it may under exceptional conditions appear in children of five or six years or even later (rachitis tarda). Since the war this "late rickets" has become very common in the children of central Europe. The disease may be manifest by the second month of life. It is most frequent from the seventh month to the end of the second year. It is usually accepted as true that the disease is never or only very rarely present at birth, but since clinically recognizable symptoms may occur very early in life, and the development of the disease is slow, it must in many children have its beginning in the earliest days of extra-uterine life.

318. **The Characteristics of the Disease.**—In many children the condition is only discovered at autopsy since the lesions have not sufficiently progressed during life to attract attention. It must be emphasized that although the diagnosis rests only upon

the manifestations in the skeleton, rickets is a disease of the entire organism and not of the bones only. The children exhibit signs which can only mean that the whole body is involved in the physiological process. They are nervous and irritable, but usually are apathetic and disinclined to play. They sleep poorly. The muscles are flabby, wasted and weak. This is not only true of the voluntary muscle but also of the smooth muscle of the gastro-intestinal tract. The ligaments are loose and lax. The children perspire freely, especially about the head (head sweats). Frequently the head is continually rolled from side to side on the pillow so that the hair may be worn off from the back of the head. There is often a more or less marked secondary anemia.

The disease may exist without symptoms. Those which are found result from the abnormality of the bony structures and the feebleness of the musculature. The children sit, stand and walk at much later periods than normal children. Although they have as much opportunity for exercise as the normal child, they do not profit by it. Weakness of the abdominal and intestinal musculature results in accumulation of gas in the intestine, and distention of the abdomen (pot belly). The teeth are late in making their appearance and decay early.

The bones are widely affected. Rickets is more severe, often, in some bones than in others, but in advanced cases every bone in the body is involved. Those that grow most rapidly suffer first. The bones of the skull and ribs are attacked early. Among the earliest signs of rickets are areas of softening in the bones of the skull (craniotabes). The junctions of the bony ribs with their cartilages become enlarged. The softened ribs are bent by atmospheric pressure and by the traction of the diaphragm during breathing so that a deep groove is formed in the chest wall along the insertion of the diaphragm. The long bones become bent and are swollen at their extremities. Bow legs and knock knees and sabre shins result from bending of the softened bones, and the wrists and ankles are swollen. On the bones of the skull masses of soft tissue beneath the periosteum give rise to the appearance of the so-called bosses or swellings. The fontanels are slow to close. In severe cases the bones may fracture or the head of the bone may be separated from the shaft. The spine may be twisted and the pelvis distorted. The resistance of these children to infections is lowered and they have sometimes an almost continuous coryza. This lowered resistance together with the deformities of the chest make them very liable to attacks

of bronchitis or bronchopneumonia, which frequently are the direct cause of death.

While the death of rachitic children is usually due to some intercurrent infection, severe rickets may be fatal of itself as Park and Howland (1) have pointed out.

319. **A Historical Survey of Rickets.**—Findlay (2) in a recent historical survey of rickets says: "In this (England) as in most civilized countries, rickets is one of the most common diseases of childhood. Further, it is probably the most potent factor in interfering with the efficiency of the race. It not only stunts the growth and causes deformities, some of which greatly increase the dangers of child-bearing in the female, but it raises considerably the mortality rate of such diseases as measles and whooping cough, and is responsible for the rejection annually of a not inconsiderable number of army recruits."

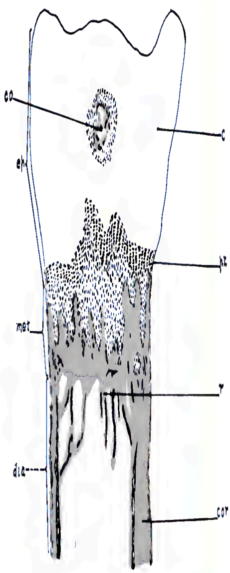
Schmorl (3) examined hundreds of children and found that 90 per cent of all who died under four years of age had had rickets. Dick (4) reported that 80 per cent of all the children in London County Council Schools had had rickets. Hess and Unger (5) found the disease present in nearly all the negro children in the negro quarter of New York, and they recently state that "all seem to agree that it occurs in more than 50 per cent of the children of the poor." Thompson (6) reports that more than 50 per cent of the children of Edinburgh, London, Glasgow and Manchester suffer from rickets. It will be readily apparent, therefore, that rickets constitutes a national health problem of first importance.

Rickets is a disease which has long afflicted the human race. It was described in its general features by Soranus in the first century of the Christian Era (7). He stated that the majority of Roman children suffered from deformity of the spine and crooked legs, and noted that this abnormality of growth was more common in the neighborhood of Rome than in other places. He said further, that the disease was unknown among the Greeks, and attributed this to the greater interest and care bestowed by the Greek mothers upon their infants, than was customary with the mothers of Rome. Defects of skeletal development of the nature of rickets appear not to have existed in Ancient Egypt.

Rickets as a clinical entity was first described in some detail by Francis Glisson in 1650 (8), and his work has become one of the classics of medical science. He described the enlargements of the ends of the long bones, the deformity of the thorax, the

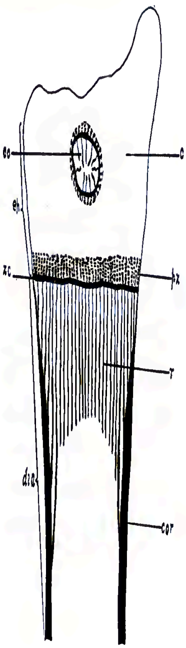
"rosary" due to enlargement of the junctions of the bony ribs with their cartilages, the abnormally large head, the protruding abdomen, the flacidity of the musculature and the generally wasted condition of the body. He pointed out that the disease was not usually fatal, and attributed the deformity to unsymmetrical growth of the two sides of the bones because of interference with the blood supply.

320. **Geographical Distribution of Rickets.**—Findlay (2) points out that rickets is almost entirely limited to the northern



Rickets

hemisphere, and that it is in great measure restricted to the temperate zone. At present it is a veritable scourge among the children of many parts of Europe owing to conditions brought about by the war. It is common in most parts of Europe except in southern Spain, southern Italy, and Portugal. It appears to be rare in the West Indies, most parts of South America, the Philippines, a large part of China, India and the Malay peninsula. Sporadic cases occur in all these places. Mellanby (9) states that in the west of Ireland the disease is unknown. Rickets is said to be much rarer among Jewish children than among other elements in the population.



Normal

Legend descriptive of illustrations of normal and rachitic bones, shown on pp. 297-298.

To show the differences between a rachitic and a normal bone. In the shaft (dia) and the center of ossification (co) of the epiphysis (ep), calcified tissue is black and osteoid tissue red. The zone of provisional calcification is absent from the rachitic bone, and the proliferative zone of cartilage (pz) is prolonged as an irregular mass of cartilage which is ragged and interdigitates with tongues of osteoid tissue. A metaphysis is formed. The cortex (cor) is thickened though the bone in it is very thin. The trabeculæ are surrounded by osteoid.

c……Resting cartilage.
co……Center of ossification.
ep……Epiphysis (head).
met….Metaphysis.
dia….Shaft (diaphysis).
zc……Provisional zone of calcification.
pz……Proliferative zone of cartilage.
T……Trabecula.
cor….Cortex of shaft.

321. **Rickets Absent from Certain Parts of the Hebrides.**—Mellanby further calls attention to the almost complete absence of rickets in the Island of Lewis in the Hebrides, although the people there live under the most intolerable hygienic conditions. He emphasizes the importance of this fact in support of the view that the disease is essentially due to faulty diet, and not to unfavorable hygienic surroundings.

It is necessary to receive statements about the geographical distribution of rickets with a certain amount of skepticism, since they are often the result of careless observation or of the inability of the observer to recognize mild cases of the disease. The statement is made frequently and accepted generally that rickets does not occur in the tropics or is very rare. As a matter of fact the disease is not at all uncommon in parts at least of Central and South America (Brazil, Venezuela, Guatemala).

322. **Views Concerning the Cause of Rickets.**—The most diverse views have been advanced regarding the cause of this disease. Many have believed it an essential concomitant of civilization. This idea is supported by the unquestioned fact that it is much more common in cities than in rural districts. It is relatively rare to-day among the less progressive peoples of the Orient and among those of tropical and subtropical regions. It is very significant from the standpoint of determining its cause, that the disease is very rare or unknown in certain places as in Ireland, and the Hebrides, and very prevalent in adjacent regions, in England and Scotland, where differences in climate or in amount of sunlight could not logically be invoked as factors which would determine the incidence of rickets. In Iceland the disease occurs very rarely, and is unknown among primitive Eskimo. Findlay states that inquiry of the Alaskan School Service revealed that rickets had recently occurred in several villages north of the Arctic circle. It was stated that the natives of these villages were living under better conditions than in former years. Because of this last statement Findlay expresses skepticism about the diagnosis. It would seem, however, that this "living under better conditions than in former years," may have been a very significant factor in causing the appearance of rickets among the children. This so-called improvement may well have included, in addition to living in a house instead of the primitive hut, a generous addition of bolted wheat flour and other cereal products, and canned goods to the diet. This point would be well worth further inquiry.

323. **Rickets Does Not Occur in Wild Animals.**—Rickets does not occur among wild animals, but is common among wild creatures kept in confinement. This is especially true of monkeys and young carnivora kept in zoölogical gardens. Dogs, especially the larger breeds, are very prone to develop rickets, whereas cats are said to remain free from the disease under domestication. This fact is of great significance, since the cat rarely fails, even when domesticated, to kill birds and small rodents in considerable numbers, and to remain in a measure on the type of diet characteristic of wild carnivora, whereas dogs are less enterprising as foragers, and rely upon the food provided by their masters. Herbivorous animals such as the horse, cow, sheep, pigs and others do not frequently exhibit skeletal defects where a pasturage is available. It will be shown later that these facts can be satisfactorily explained on the theory that the diet is the most important factor in the etiology of rickets.

324. **Relation of Breast Feeding to Incidence of Rickets.**—Rickets was formerly much more common among the poorer classes than among the well-to-do. It occurs much more frequently in the winter and spring than at the other seasons, and is much more prevalent among bottle-fed infants than among nursed infants. It occurs not infrequently in infants who are breast-fed. It is not uncommon to see severe rickets develop in negro children who are fed almost entirely at the breast. The following table from data collected by Miss Ferguson (2) shows the relation of rickets in the children of Glasgow to length of time at the breast in months.

	Marked Rickets (250 Children)		*Slight Rickets (200 Children)*		*Non-rachitic (200 Children)*	
	No.	*Per Cent.*	*No.*	*Per Cent.*	*No.*	*Per Cent.*
Not at all......	58	23	32	16	25	12.5
1 month.......	9	4	6	3	7	3.5
2 months......	12	5	5	2.5	3	1.5
3 months.......	12	5	9	4.5	6	3
4-6 months.....	17	7	12	6	10	5
7-9 months.....	17	7	25	12.5	33	16.5
10-12 months...	54	21	57	28.5	66	33
Over 12 months	70	28	54	27	49	24.5

Since breast-feeding has been generally regarded in the past as assurance that the diet of the infant will be of satisfactory

quality, data such as are recorded in the table on page 300 would be interpreted by most people as a strong support for the view that the character of the diet has little or nothing to do with the etiology of rickets. In recent years, however, there has been brought to light more and more evidence of an experimental nature, which casts doubt upon the adequacy of breast milk as a food, where the diet of the mother is not wisely chosen.

The studies of Ferguson further emphasize the importance of the time of year in influencing the development of rickets. Of 349 children observed by her, 232 ceased to thrive between December and May, against 117 who developed rickets during the other half of the year. Thompson (6) has also recently emphasized the effect of the winter season in inducing this disorder.

325. **Some Regard Diet, Others Hygiene, as the Main Factor in Inducing Rickets.**—No unanimity of opinion exists among students of rickets concerning its cause. Heredity, dietetic errors, faulty hygienic conditions, infections of a microbial or other nature, and disturbances of the endocrin glands, have all been incriminated as the causative agents. At the present time two schools of investigators are essentially monopolizing the field in the study of this disease. One holds that it is essentially a condition brought about by errors in the diet, although admitting that unfavorable living conditions of any kind may play a rôle in that they depress the metabolic functions and cause the child to show more readily the effects of faulty nutrition than it would under more favorable conditions. The other school supports the view that hygienic conditions, especially lack of sunlight, and not dietetic factors, play the dominant rôle in the etiology of the disease. It seems possible to offer an explanation which brings into harmony most of the observations upon which the diverse interpretations have been placed.

326. **Mellanby Suggests That Rickets Is Due to Lack of Fat-Soluble A.**—In 1919 Mellanby (9) reported experiments which excited great enthusiasm among investigators of nutrition problems. He was able to show that certain diets produced a condition of the bones of young puppies which he believed to be identical with rickets in the human being. Radiographs showed a decrease in the density of the bones. The ends of the shafts were cupped and much enlarged and were more or less ragged in appearance. The translucent (to X-rays) area between the shaft and the center of ossification in the head of the bones was increased in depth. Mellanby regarded röntgenograms of this

sort as sufficient evidence of rickets. As will be made clear later the radiograph only shows that the bones were not normally developed, but gives no information concerning the exact nature of the lesion such as can be learned only by histological examination of stained sections. The most striking point brought out by his experiments was the protective function of butter fat and cod liver oil in preventing the development of rickets or some similar condition. One diet which produced rickets in pups was composed of skimmed milk 175 c.c.; white bread *ad libitum*; linseed oil 10 c.c.; yeast 10 grams, and common salt 1-2 grams. The addition of 10-20 grams of butter served to so improve the nutrition of the animals that rickets did not develop. Mellanby drew the conclusion from his studies, that such fats as furnish fat-soluble A are protective against rickets, whereas vegetable fats which do not contain appreciable amounts of this substance, are of little value in this respect. He was therefore inclined to identify the fat-soluble A, or some substance having a similar distribution, as a specific anti-rachitic substance.

Mellanby compared two diets which Ferguson (2) had described as typical of rachitic and of non-rachitic families respectively in Glasgow. These are so instructive that they are reproduced here in tabular form. It will be evident to anyone who has become familiar with the specific dietary properties of the individual food-stuffs and with the nutritive requirements of an animal with respect to calcium, phosphorus and fat-soluble A, and with the importance of having proteins of high biological value, that one is not justified in interpreting the results of restricting human beings or animals to one or the other of these two types of diets, as turning upon their content of fat-soluble A, or similar substance which might play an important rôle in the etiology of rickets.

Average Consumption Per "Man" Per Day of the Chief Articles of Diet in Grams.

(1) rachitic families. (2) non-rachitic families.

	(1)	*(2)*		*(1)*	*(2)*
Flour	387.9	376.2	Other cereals	15.6	26.9
Potatoes	291.0	236.8	Margarine or butter	32.6	38.5
Milk	256.0	309.0	Fish	15.7	35.9
Meat	89.1	92.6	Eggs	15.1	30.4
Sugar	91.4	84.0	Cheese	6.7	8.2
Oatmeal	40.4	36.0			

327. A Comparison of a Rachitic and a Non-Rachitic Dietary.—It is very significant that the quantities of milk, eggs, cheese, fish and butter contained in diet (2) over diet (1) was effective in preventing the occurrence of rickets. Ferguson did not consider the differences in the composition of these types of diets sufficient to support the view that the diet had any importance as a factor in the production of rickets. When these diets are evaluated in the light of present day knowledge, it is easy to see that neither is of very good quality for the promotion of growth or the maintenance of health, but that diet (2) is distinctly better than (1).

A similar comment may be made concerning the rachitic diet described above, which became non-rachitic on the addition of butter. The basal diet which induced rickets was poor. One factor in which it was distinctly below the optimum was its content of fat-soluble A. The addition of this substance improved the diet, not only because of its enhancement in fat-soluble A, but because any other defects in the diet would become manifest in the condition of the animals, to a lesser degree when more of the needed fat-soluble A was present. We have already seen that any single factor in a diet may be well below the optimal in quality, without its effects becoming apparent. They appear, however, when another factor is reduced in quality so as to increase the total burden which the tissues must tolerate, in the way of badly constituted nutriment.

Mellanby's hypothesis would seem to derive support from the century long use of cod liver oil as a therapeutic substance in the treatment of rickets and from such studies as those of Schabad (10), who showed that the exhibition of cod liver oil increased retention of calcium salts by the body.

328. Hess and Unger's Experiments on Infants with Fat-Poor Diets.—After the appearance of Mellanby's paper his opinion was at once accepted as resting on sound experimental evidence. The Medical Research Committee of Great Britain accepted it and gave it wide publicity in their bulletin (9). Hess and Unger (5), who had earlier stated their view that the long accepted use of cod liver oil in the therapy of rickets was based upon sound experimental data, and that in their experience it had proven a specific in the treatment of rickets, now came forward with the publication of the results of feeding experiments on infants with diets very deficient in fat-soluble A (11). The diet consisted of dried skim milk 180 grams; dissolved in ten

times its weight of water; to this was added 30 grams of cane sugar, 15 c.c. of orange juice, 30 c.c. of autolyzed yeast, and 30 c.c. of cottonseed oil. This was fed to infants ranging from four to nine months of age, for a period of five to nine months. Growth at a fairly satisfactory rate was observed, and no evidences of rickets were apparent. The conclusion was drawn that fat-soluble A is a factor of minor importance in human nutrition. This view is at variance with the remarkable studies of Mori (12) and of Bloch (13) as well as of those of Wells (14), which leave no room for doubt that butter fat and cod liver oil furnish something which may under acute conditions cause prompt recovery from ophthalmia, brought on by malnutrition.

The diet employed by Hess and Unger cannot be regarded as a satisfactory one to which an infant may safely be confined, notwithstanding their observation that their subjects grew during the experimental period. There is every reason to suppose that they were brought into a state of nutritional instability as the result of being confined to the diet. This was very satisfactorily constituted except for its shortage of fat-soluble A, and judging from experience with animals they should, therefore, have been able to tolerate for a considerable period this defect in their dietary, but not necessarily without injury in some degree. McCollum and Davis (15) had shown that skim milk powder contains approximately half the fat-soluble A that was contained in the whole milk from which it was prepared. Hopkins (16) has expressed a similar view as the result of his investigations. No conclusions are warranted from the data of Hess and Unger other than that young children can live and grow as their graphs show them to have done. They throw no light on the relation of fat-soluble A in its relation to bone growth, or the nutritive needs of the human infant for this dietary factor, since their experimental diet was by no means so deficient in fat-soluble A as they supposed it to be.

Very recently Hess and Unger (17) have abandoned the view that rickets is due to dietary defects, and have adopted the view that hygienic factors, especially sunlight, play a dominant rôle in determining the seasonal variation of this disorder. They base their belief upon the evidence afforded by röntgen ray pictures, which showed that illumination of infants suffering from rickets, with ultraviolet rays from a mercury vapor lamp, caused the deposition of calcium phosphate in the zone of primary calcification of the long bones. Hess and Unger offer no

explanation for the mechanism of the action of cod liver oil as a specific therapeutic agent in the treatment of rickets in their earlier studies.

329. **Exercise as a Factor in Preventing Rickets in Pups.**—Findlay (18) has continued as has also Paton (19), to emphasize that the opportunity which is afforded for pups to exercise is the determining factor as to whether or not they will be likely to develop rickets. Recently these investigators have been inclined to accept infection as playing the major rôle in the production of rickets.

It will be evident to one who gives careful scrutiny to the recorded experimental studies of this subject, that as yet no thoroughgoing research has been carried out for the purpose of making clear the etiology of rickets. Shipley, Park, Simmonds and McCollum (20) have approached the problem from an essentially new viewpoint. They observed in the course of extensive studies of nutrition problems with a large rat colony, that certain animals whose diets were faulty in one or more respects, developed a condition which presented the gross appearance of rickets both as respects external appearance and conditions which could be observed at autopsy. They were convinced that only by a most elaborate study of the subject, that is, by systematically varying the composition of the diet with respect to one or more factors, and by means of careful histological studies of the bones of their animals, could one expect to reveal the relation of the diet to the disease. Since their animals were all kept in a north-east room, into which sunlight enters only in small amount, and all of the colony were under essentially uniform conditions as respected illumination, temperature, ventilation and opportunity for exercise, they were convinced that any differences which could be demonstrated in the histological structure of the bones must be due to the character of their experimental diets, which formed the only variable. Radiographs cannot be of much value in studies in this kind since they do not reveal the nature of the anatomic changes which take place under experimental conditions. These studies have progressed far enough to establish certain important facts concerning the etiology of rickets.

330. **Sequence of Events in the Growth of Bone.**—The growth of a bone in length is due to a definite sequence of events which transpire at the junction of the shaft of the bone (diaphysis) with its head (epiphysis). The shaft is composed of

growing bone, the epiphysis of cartilage which is largely in a resting state. As the animal grows the cartilage of the epiphysis is converted into bone through (a) encroachment on it of the bony shaft and (b) through the expansion of one or more centers of ossification which form in it. The process of growth in length of the shaft is the same which results in the expansion of the centers of ossification in the epiphysis.

The cells of the resting cartilage have no particular arrangement until they come within a short distance of the shaft or center of ossification. The cartilage cells then arrange themselves into columns parallel to the long axis of the shaft or the radii of the ossification center. This columnar zone is known as the "proliferative cartilage." Lime salts are deposited in the matrix separating the cells of the thin layer of cartilage in contact with the shaft. This is known as the zone of provisional calcification. Cartilage cells in this zone lie in a matrix which is like a calcified honey-comb. As the shaft grows tiny blood vessels sprout evenly from it and each vessel opens a single compartment in the calcified honeycomb. The cartilage cell is freed to degenerate or to become an osteoblast or bone-forming cell. Large numbers of osteoblasts follow the blood-vessel sprouts into the cartilage. These settle on the spicules of calcified matrix which remain after the cartilage cell capsules are opened. These spicules furnish cores about which the trabeculæ of bone in the shaft are built. The osteoblasts on the spicules of calcified matrix bury themselves in a tissue known as osteoid which they manufacture. This receives a deposit of lime salts and becomes bone.

Growth in thickness of the shaft is accomplished by cells in a thick layer of connective tissue which surrounds the shaft and is called the periosteum. These connective-tissue cells are transformed directly into osteoblasts and lay down bone in layers beneath the periosteum. During growth, and to a lesser extent after growth has ceased, the structure of a bone is subject to constant change to meet the requirements of exercise and changing conditions of stress and strain. Old bone is constantly being removed (resorption) and new bone is always being formed. In a normal, healthy bone these processes are always in a dynamic equilibrium.

331. Abnormal Histological Changes in Rachitic Bones.—In the rachitic bone all these processes of growth and the maintenance of equilibrium are abnormal. Calcium salts are not

deposited in a normal way. In a normal bone the junction of the cartilage with the shaft forms a straight, regular line. In the rachitic bone it is ragged because there is no provisional zone of calcification and the cartilage is invaded by large tufts of blood-vessels from the shaft which destroy it irregularly. At the same time masses of cartilage persist where they should be destroyed and islands remain cut off from the main body of the tissue. Osteoid is not calcified as it is formed either in the trabeculæ or by the periosteum, so that the bones become soft. The animal attempts unsuccessfully to compensate for the weakness due to the lack of lime salts by producing osteoid tissue in abnormal amounts, especially at points subject to stress and strain (the curved side of the bone and at the insertions of muscle and tendons). This over-production of osteoid and cartilage causes irregular enlargement of the bones and their weakness consequent upon the lack of lime salts results in bowing and fracture. Because of the abnormal growth at the end of the shaft a zone known as the rachitic metaphysis forms, which consists of blood-vessels, connective tissue, osteoid, marrow elements, and cartilage cells in all stages of degeneration and change into other tissue. The osteoid formed shows little sign of being absorbed in rickets as it is commonly seen. The balance of forces has swung in the direction of apposition and persistence of cartilage.

332. **Recent Investigations on the Cause of Rickets.**—The investigations of Shipley, Park, Simmonds and McCollum have shown that when the diet is satisfactory in every respect except for a deficiency of calcium, the phosphate content and content of fat-soluble A being near the optimal, changes take place in the skeleton which bear a fundamental resemblance to rickets as it occurs in the human being. There is a tendency to increased persistence of the proliferative cartilage of the epiphysis. The cartilage becomes invaded by blood-vessels from the marrow of the shaft. There is failure to deposit calcium salts in the intercellular substance of the cartilage, which forms the initial feature of the process of normal calcification. A rachitic metaphysis is formed. There is likewise over-production of osteoid tissue. The gross deformities in young rats maintained on such defective diets (deficient only in calcium) cannot be differentiated from those seen in rickets.

There are, however, decided differences in the histological picture seen in bone sections derived from animals selectively

fasted for calcium alone, as compared with those ordinarily seen in rickets. It has been pointed out that normally the band of proliferative cartilage consists of cells which are arranged in columns. In true rickets this orderly arrangement is lost, and the cartilage cells become irregularly disposed. In the animals deprived of calcium, but supplied with all other dietary essentials in normal amounts, the orderly arrangement of the cartilage cells is not disturbed, notwithstanding the formation of abnormal amounts of osteoid, and the development of the metaphysis. There is also evidence that resorption of bone and osteoid in the shaft is rapid under these dietary conditions.

When calcium carbonate, in appropriate amount, is added to such diets as produce the picture described above, none of the abnormalities described occur. When, on the other hand cod liver oil is included in the diets which are deficient in calcium, but in no other respect, and the deficiency is sufficiently marked to cause the rickets-like condition to develop, the bones remain essentially normal and no metaphysis forms. When the cod liver oil is administered after the pathological changes due to deprivation of calcium have developed, healing of the lesion results. The calcium necessary for deposition in the zone of primary calcification under these circumstances appears to be borrowed from the shaft, for this becomes osteoporotic, or fragile owing to resorption of its mineral salts.

The administration of butter fat instead of cod liver oil to animals *which are deprived of a sufficient amount of calcium*, does not protect them in the way that cod liver oil does. Even large doses (20 per cent of the food mixture) exerts but a feeble protective action. It must be concluded, tentatively, therefore, that cod liver oil is rich in some substance which is intimately concerned with bone growth, which is not abundant in butter fat, and that the evidence available at present, points to the possible existence of a separate dietary factor analogous to the recognized vitamins, which can be recognized by its effects on the changes in the bones of animals which have been prepared for a period by restricting them to diets which lead to the development of rickets.

When young rats are restricted to diets which contain the normal amounts of calcium and of phosphate, a deficiency in fat-soluble A causes changes in the bone of a pathological nature. This factor alone cannot, however, be responsible for the development of rickets. This statement also applies to a relative

shortage of the hypothetical anti-rachitic factor which we tentatively suggest is distinct from fat-soluble A, and abundant in cod liver oil. A specific starvation for this substance cannot of itself produce rickets.

When in the nutrition of young rats, a diet is employed which is deficient in utilizable phosphorus compounds and also in the organic factor which exerts an anti-rachitic effect, there is produced a pathological condition of the skeleton which bears fundamental resemblances to rickets, but differs from rickets in certain respects. The chief difference consists in the presence of scattered or irregular deposits of calcium salts in the metaphysis and cartilage. The appearance of histological sections of the bones of these animals closely resembles those of animals which have suffered from rickets but in which healing of the lesion is in progress. The addition of a suitable amount of the phosphate ion to such a diet, the deficiency of the organic factor still existing, results in the prevention of the development of the changes of a rickets-like nature, though the bone is not normal.

The remarkable effect of the administration of cod liver oil to animals which are deprived of sufficient calcium, in protecting them from the detrimental effects of such deficiency—a protection which is not afforded by four or five times the amount of butter fat necessary to entirely meet the needs of the growing rat for fat-soluble A, when its diet is satisfactorily constituted with respect to calcium and phosphate, makes it imperative that we accept the view that there is an organic factor which exerts an anti-rachitic effect, and is concerned in the normal nutrition of the bones.

333. **Three Factors Operate in the Etiology of Rickets.**—It will be seen from the foregoing, that three dietary factors at least are concerned primarily in the development and normal metabolism of the skeletal tissues. These are the phosphorus and calcium content, and the content of the organic substance which we may provisionally designate as the anti-rachitic substance, although this is not an entirely satisfactory term since this substance is not a preventive of rickets in the sense that the anti-beri-beri substance or the anti-scorbutic substance are respectively preventives of beri-beri and scurvy. The organic substance under discussion may exert an anti-rachitic effect, but so also may phosphorus or calcium, depending on the peculiar constitution of the diet.

Rickets, it will be seen, is not a deficiency disease in the same sense as are beri-beri, scurvy or the ophthalmia of dietary origin. Beri-beri, scurvy and ophthalmia, so far as we can now see, are due to specific starvation for one (possibly more) organic substance, peculiar to each disease, whereas rickets has at least three etiological factors, disturbances of the ratios among which will effect the structure of the bones.

It is now easy to appreciate, in the light of the experiments just described, that rickets must be studied in a special way if satisfactory results are to be secured. Isolated observations cannot well be correlated and interpreted. It is essential that the effects on the structure of the osseous system, of deviation from the optimal relations with respect to all factors which can be shown to enter into the etiology of rickets and related disturbances of bone growth, be systematically studied in a very comprehensive way before a complete explanation can be given of this most interesting problem in pathology.

334. **The Ratio Between Calcium and Phosphorus in the Diet is Very Important.**—A discovery of great importance in this connection was recently made by McCollum, Simmonds, Shipley and Park (20) who observed that *the ratio between the concentration of calcium and of phosphorus in the diet may, within certain limits, be of greater significance to the welfare of an animal than the absolute amounts of these substances which the diet contains.*

335. **Sherman and Pappenheimer's Observation on Rickets.** Sherman and Pappenheimer (21) have recently described the production of rickets by a diet deficient in phosphorus, and its prevention by the administration of a phosphate. Their data would lead one to the conclusion that the disease is brought about by phosphorus starvation. The isolated observation of these investigators is of special interest in that it is explainable on a very different basis from that which they had in mind. Sherman and Pappenheimer fed groups of young rats on the following diets, and with the results noted:

Wheat flour, sodium chlorid, 2%.	No rickets.
Wheat flour, sodium chlorid, 2%, Ca Lactate, 3%.	Rickets.
Wheat flour, sodium chlorid, 2%, Ca Lactate, 3%, K_2HPO_4, 0.4%.	No rickets.

Instead of lack of phosphorus, *per se*, being the cause of the rickets in their animals, McCollum, Simmonds, Shipley and Park (20) regard the cause as due to *an unfavorable ratio between the*

calcium and phosphorus, in the absence of sufficient of the organic factor which plays a rôle in the production of this syndrome. The reasoning on which this conclusion rests was based upon experimental data which is of great interest in illustrating one of the several dietary situations which may give rise to rickets or similar conditions. The results of feeding the following diets will illustrate this principle.

Ration 3127		Ration 3133	
Rolled oats	40.0	Rolled oats	40.0
Gelatin	10.0	Gelatin	10.0
Wheat gluten	7.0	Wheat gluten	7.0
NaCl	1.0	NaCl	1.0
KCl	1.0	KCl	1.0
$CaCO_3$	2.0	$CaCO_3$	2.0
Dextrin	39.0	Dextrin	38.5
		Butter fat	0.5

Ration 3127 was markedly deficient in phosphorus and in fat-soluble A (anti-xerophthalmic substance), but was otherwise well constituted. Its proteins were of good quality, and its content of calcium not far from the optimum. Young rats fail to grow on this food, and develop severe ophthalmia. They cannot live many weeks on this diet because of the severity of the ophthalmia which develops.

Ration 3133 is essentially like Ration 3127, but contains 0.5 per cent of butter fat, which was added to defer the onset of ophthalmia and prolong the lives of the animals. This amount of butter fat did not suffice to protect against ophthalmia, but delayed its advent and diminished its rate of progress, and therefore increased the life and made possible, presumably, a greater amount of growth in the skeleton than was possible on diet 3127.

Both of the rations just described, in which the calcium content was optimal and the phosphorus and fat-soluble A very low, produced in young rats a pathological condition essentially identical with that found in human subjects of rickets. The lesions were more severe in animals fed Ration 3133 because of the small addition of butter fat, which functioned as described above.

336. **Excessive Calcium Content in the Diet May Play a Role in Bone Pathology.**—The following diet produces the most extreme degree of rickets:

Ration 3143

Wheat (entire kernel)	33.0
Maize (entire kernel)	33.0
Gelatin	15.0
Wheat gluten	15.0
NaCl	1.0
$CaCO_3$	3.0

The dietary faults in this mixture are of a threefold nature. It contains about twice the optimum amount of calcium, and is very deficient in phosphorus and in fat-soluble A. The calcium: phosphorus ratio differs markedly, therefore, in this diet from that of the other diets described (3127 and 3133). The severity of the lesions produced were much greater than are ever seen in human cases of the disease. A small amount of fat-soluble A was furnished by the wheat and maize.

The results of feeding young animals on these diets in which there were faulty proportions between the calcium and phosphorus and a deficiency of fat-soluble A, are seen to depend in their severity upon the deviation from the optimal of the Ca:P ratio. We have repeatedly observed that the addition of excessive amounts of calcium carbonate to diets which were deficient in phosphorus and in fat-soluble A, induce most pronounced disturbances in the growth of the bones. It appears from these studies, that it is of more importance to the individual to maintain the proper ratio between the calcium and phosphorus than to deviate from the optimal concentrations of these two elements, when the ratios are more favorable.

337. **Discussion of Sherman and Pappenheimer's Experiments.**—In the light of these experiments it is possible to understand the results of Sherman and Pappenheimer, and it is necessary to place upon them a different interpretation from that of these investigators. This matter is so important, not only from the standpoint of the etiology of rickets, but as an illustration of the necessity of very elaborately planned series of experiments in order that error may be avoided, that a short discussion of them will be of value.

Patent flour is one of the most deficient foods which enters into the human diet, being exceeded in this respect only by isolated foods such as starch, sugars, fats or polished rice. Bolted flour is rather poor in protein and this is of rather poor quality. It is very deficient in calcium, phosphorus, sodium, chlorin, iron and possibly also in potassium. The only essential inorganic

element which it probably contains in amount sufficient to meet the needs of an animal is magnesium. Bolted flour is also very deficient in the anti-neuritic substance (water-soluble B) as shown by the frequent occurrence of beri-beri among the people of Labrador and Newfoundland, where bread from this source is a principal article of food. It is exceedingly poor in fat-soluble A, and in the organic factor playing a rôle in the prevention of rickets. From the standpoint of human nutrition it is important also that it lacks entirely the anti-scorbutic substance. The basal ration employed by Sherman and Pappenheimer was deficient in all the factors enumerated above. In the presence of so considerable a number of defects in the ration it was obviously impossible to be certain which were operative in the production of the disease. In the light of their experience, McCollum, Simmonds, Shipley and Park interpret the data of Sherman and Pappenheimer as follows (20).

When calcium was added to the basal ration a marked disproportion in the calcium-phosphate ratio was produced, the calcium being nearly optimal and the phosphorus very low. Fat-soluble A (an anti-rachitic substance) was almost lacking, and the conditions were such under which we should expect severe rickets to develop. When neither calcium nor phosphorus were added, the content of both these elements in the diet was that contained in bolted wheat flour, and the ratio was more nearly the optimum than after the calcium addition, and, accordingly, osteoporosis and not rickets should have developed. They did not state whether osteoporosis existed. The animals were sorely in need of calcium, yet its addition under these peculiar conditions caused the development of the syndrome of rickets which they would otherwise have escaped. The situation is analogous to the effect of adding 0.5 per cent of butter fat to diet 3133. The animals needed the fat-soluble A which it contained, but its addition under the peculiar conditions of composition of that diet increased the severity of the rickets which developed. This principle has not hitherto been conceived of by nutrition investigators, but it is one of fundamental importance. When the potassium phosphate in the experiments of Sherman and Pappenheimer, was added, the Ca:P ratio was again made more favorable and rickets was prevented. In this case, the diet was made to contain fairly satisfactory concentrations of both these elements, which tended to promote normal bone development.

338. Ratios Between Calcium and Phosphorus More Im-

portant Than Their Absolute Amounts.—*Apparently in the rat the profound disturbances in the deposition of lime salts in cartilages and bone and the changes in the cells of those tissues which give rise to the pathological complex known as rickets, may be produced by disturbances in the diet of the optimal ratio within certain limits between calcium and phosphorus, in the absence of a sufficient amount of the organic substance contained in cod liver oil to prevent them. It would seem from the results of a large number of experiments now available, that the physiological relation in the diet within certain limits between the two elements is of much greater importance in insuring normal calcification, than the absolute amount of the salts themselves* (20).

339. **Protective Action of the Organic Factor Concerned in the Causation of Rickets.**—The effect of the administration of the organic factor which has several times been mentioned as playing a rôle in the etiology of rickets, is very easy to demonstrate by properly planned experiments. If one places young rats on a diet which is too rich in calcium and too poor in phosphorus and in fat-soluble A, they develop a condition in their bones which is characterized by the absence of calcium salts in the zone of primary calcification. The calcium is available in abundance and a certain amount of phosphorus is present in the food, but owing to the unfavorable ratio and the absence of the organic substance in question deposition of calcium salts is not possible. When young rats are prepared by such a diet so as to insure that there will be a calcium-free zone in their bones, they respond with calcium deposition at once when the deficient organic substance is exhibited in the diet. Two per cent of cod liver oil administered to such rats leads in the course of five to ten days to the appearance in sections cut longitudinally through the bones, of a fine line of calcium phosphate, which represents the beginning of healing of the lesion. Butter fat, even to the concentration of 50 per cent of the food mixture, fails under the condition of this test, to stimulate calcium phosphate deposition as effectively as does 2 per cent of cod liver oil. With this technic it is now possible in a simple and easy manner to test the anti-rachitic property of any food substance with respect to this organic factor. By changing the composition of the diet on which the animals are prepared, so that the calcium-free condition is determined by some other factor in the diet, e.g., calcium or phosphorus, it is possible to test the

anti-rachitic effect of each of the dietary factors which are concerned with the etiology of rickets. This test is by far the most satisfactory one yet devised for the detection or approximate estimation of any of the vitamins.

340. **Further Observations on Changing the Ratios Between Calcium and Phosphorus in the Diet.**—The effect of changing in the direction opposite to that described above (Rations 3127, 3133 and 3143) the ratio between the calcium and phosphorus has been tested. A diet consisting of cereal grains, and legume seeds does not induce any growth because it is too poor in calcium. It is likewise deficient in phosphorus, but not in so marked a degree as in calcium. The content of fat-soluble A is also far below the optimum and its proteins are not of the best quality. The diet in question is No. 2638, described by Shipley, Park, Simmonds and McCollum (20).

Ration 2638.

Wheat	30.0
Maize	30.0
Polished rice	10.0
Rolled oats	10.0
Peas	10.0
Navy beans	10.0

If this diet is supplemented with common salt, calcium and fat-soluble A, it supports good growth and fair fertility. The animals are not normal, however, as is shown by subnormal fertility, high infant mortality, the short span of life, and the deterioration of families of animals restricted to it through several generations.

When young rats are confined to this diet without supplementing its calcium and protein content, they cannot grow, and are brought into a state of nutritional instability. They do not constantly develop distinct rickets, although the bones are not entirely normal and frequently suggest rickets. The addition of 10 per cent of casein, a phosphorized protein, enhances the food both with respect to phosphorus and amino-acids, yet when this is done severe rickets-like changes promptly develop provided no calcium is added to the diet. This is interpreted as a demonstration that addition of phosphorus, but *without exceeding a concentration which is about the optimum under conditions where more calcium were available*, may cause damage, when it leads to the establishment of an unfavorable quantitative re-

lation between these elements. When casein and a calcium salt are added simultaneously, the diet is greatly enhanced and the bones tend toward the normal structure. They are, however, somewhat osteoporotic.

341. **Rickets Is Essentially a Disease of Dietary Origin.**—From what has been said of recent developments in the study of rickets, there can no longer be any doubt that it is a disease which is essentially due to nutritional disturbances, and that dietetic errors play the dominant rôle in its etiology. It is also clear that at least three dietary factors, calcium, phosphorus and an organic substance which is more abundant in cod liver oil than in any other substance known, are especially important in that rickets will develop unless proper amounts of these be furnished to the growing animal. Other factors may favor or interfere with the development of the disease.

342. **The Calcium and Phosphorus Content of the Blood in Health and in Rickets.**—Howland and Kramer (22) have recently reported studies on the composition of the blood with respect to phosphorus in normal and in rachitic children which are of great interest in this connection. Whereas the content of calcium in the blood remains markedly constant in health and in most diseases, the phosphorus may vary greatly. The blood of children contains 10-11 mgm. of calcium per 100 c.c. of serum. It falls below this level only in tetany, which condition is apparently directly brought about by the reduction of the calcium content of the body fluids. The serum of adults contains 9-10.5 mgm. of calcium per 100 c.c. The red corpuscles contain no calcium (22).

The inorganic phosphorus content of normal blood of children is, according to Howland and Kramer, about 5.4 mgm. per 100 c.c. of serum. The serum of adults contains but 2.1 mgm. of inorganic phosphorus per 100 c.c. In rachitic children the inorganic phosphorus content of the serum may fall as low as 0.8-2.9 mgm. per 100 c.c. of serum. It is remarkable that on the administration of cod liver oil to such children the inorganic phosphorus content of the serum at once rises to the normal or above. It is highly suggestive that the heightened concentration of phosphorus in the serum may be the cause of the resumption of deposition of calcium phosphate in the bones in rickets. There can no longer be any doubt that cod liver oil possesses a pronounced therapeutic value in the treatment of rickets, both in human and animal subjects.

343. Why is Rickets Common in Some Places and Rare in Others?—By this time it will have become apparent to the reader why rickets is common in those parts of the world where milled cereal products, tubers and muscle meats form the principal components of the dietary. Such a diet has repeatedly been shown to be inadequate for the production of satisfactory milk by a lactating mother. When we consider also that the manufacture and use of proprietary infant foods, most of which contain large proportions of cereal products, has grown to vast proportions, and that the practice of introducing very early cereals into the diet of infants, with a consequent displacement of milk, is all but universal in recent times, it is easy to understand how rickets would be expected to be common. In fact, the successful feeding of a young omnivorous animal during infancy and adolescence is a very difficult matter with which to succeed well. Young carnivora in a wild state eat glandular organs and chew soft bones as soon as they take their first steps in independence of the mother's milk, and under these conditions do not develop skeletal abnormalities. When kept in confinement and fed upon muscle meat, body fat, and a bone so large and hard that little can be gnawed from it, they invariably develop rickets (23). Young carnivora are now successfully reared in a few places by supplying them with liver, flat bones containing much red marrow, fat, and at intervals of a few days with small birds or mammals which they can entirely consume. Confinement does not seriously interfere with the development of young lions under such conditions of feeding.

Young herbivora, on the other hand, begin very early to eat tender leaves of grass, and long before they have been deprived of their milk supply have become consumers of large amounts of forage plants. This type of diet suffices for the normal development of the skeleton.

It is very different with the human infant, and with certain domestic animals which are fed an omnivorous type of diet. The human infant is nursed by a mother whose diet tends to be limited to the milled cereal, tuber and muscle meat type but with just enough milk, cream, and green vegetables to prevent the development of spectacular breakdown in her nutritional processes. Her milk is defective in some degree. The nursing period of the infant is frequently shortened for the sake of the interest of a poorly nourished mother. Milk which is fed as a substitute for breast-feeding is usually modified by dilu-

tion and the addition of cereal water, or proprietary foods having a cereal basis. There can be no question that the modern practice of modifying milks for infant feeding represents one of the most gigantic and tragic examples of persistent blundering of which civilized man is guilty. Fortunately the time seems near at hand when any manipulations to which cow's milk is subjected for feeding infants will be carried out with knowledge of what is being done, and the mistake of concocting mixtures which are entirely unsuited for the nutrition of the growing child be avoided.

344. **Suggestion of Cause of Occurrence of Rickets in Dogs but Not in Cats.**—Young dogs which are fed essentially the same food that man is now subsisting upon in Europe and America are prone to develop rickets, whereas cats, because of their tendency to prowl about in search of birds, rodents and other small creatures, which they destroy in large numbers, escape the disease. Their diet remains similar to that of wild carnivora, because they cannot be domesticated sufficiently to lead them to discontinue the practice of hunting. The dog adapts himself much more readily to domestication, and accepts his food from his master. In many instances this does not now prove satisfactory for the promotion of normal growth in the skeleton, and rickets is, therefore, of frequent occurrence.

345. **Why Are the Eskimos and Lapps Free from Rickets.**—The Eskimo, the Icelanders and the Lapps are free from the disease, or were until contact with the world through commerce changed the dietary habits of some of them. The changes which have in certain instances brought about the appearance of rickets, represent essentially the substitution of a considerable amount of milled cereal products, molasses, syrup, legume seeds and canned seed products, for a part of their primitive kinds of foods. In their primitive condition these were all essentially carnivorous in their dietary habits.

346. **Rickets Rare in Iceland.**—Iceland was settled in the ninth century by colonists from Ireland and from Scandinavia. They took with them cattle and sheep, and soon developed a considerable animal industry which flourishes today. Agriculture did not yield a return for labor, and accordingly the people of the island subsisted for generations essentially upon milk, mutton, fish, birds' eggs at certain periods of the year, and wildfowl. Under such living conditions they remained a vigorous people, but they have suffered from deterioration of the teeth

during the last seventy-five years. It is during this period that they have engaged most extensively in commerce. Parallel with the exportation of their local products and the importation of cereals and other foods of the type which have come to compose so large a part of the diet of the urban population of Europe and America in recent decades, they have become more and more afflicted with dental caries. Stefánsson (24) secured 96 skulls from a cemetery in Iceland dating from the ninth to the thirteenth centuries, and presented them to the Peabody museum of Harvard University. These have been described by Hooton (25), who found no certain evidence of caries in any of the teeth. Several teeth were broken but none were decayed. The teeth of the Lapps are essentially perfect as are those of the Eskimo in their primitive condition on a carnivorous diet.

347. **The Teeth in Rickety Children.**—The teeth are related to the skeleton and their growth and permanence are governed probably by somewhat similar laws of nutrition as are the bones. It is certain that in rickets the child fails to develop sound teeth having dense and faultless enamel, and that the roots of the teeth do not develop as they should. There has been very serious deterioration of the teeth of civilized people in many parts of the world during the last century, especially in parts of England and North America and the British overseas dominions. This has been variously attributed to the eating of cooked food, soft food, failure to properly clean the teeth, etc. Mouth hygiene has recently enjoyed great popularity, and the slogan "a clean tooth never decays" is frequently seen, especially in the advertisements for tooth pastes and tooth brushes. While commendable as a general hygienic measure, mouth hygiene doubtless has little, if anything, to do with the preservation of the teeth. All measures hitherto proposed, which stress cleanliness and prompt repair, do not get at the root of the evil. *The development during very early life of a sound set of teeth is the most important factor in preventive dentistry.* This is not so much dependent on the softness or hardness of the food, in infancy and very early childhood, as it is on the composition of the diet. If this is not adjusted in an entirely satisfactory manner, the bones and teeth will be poorly developed, and decay of the teeth in early life is then unavoidable. Chewing hard foods is, however, an important measure for insuring the development of the tissues immediately surrounding the roots, and for developing the jaws.

348. **Primitive Man Had Neither Rickets Nor Decayed**

Teeth.—In the National Museum at Washington there are several hundreds of skulls of Indians who lived between two hundred and three hundred years ago. They are from the Aleutian Islands down the Pacific coast through Honduras and Yucatan, into Peru and across to the South Sea Islands. Only a single tooth showed dental caries in the entire collection. Among these primitive peoples the diet was excellent from the standpoint of chemical completeness, and bone defects and bad teeth were unknown or nearly so. The introduction of large amounts of cereals and of tubers into the diet by civilized and urban populations has resulted during the last century in rapid falling off in physical stamina and increase in skeletal defects.

349. **Prevalence of Decayed Teeth Among American Children.**—Butler (26) points out that an examination of 7,059 children in West Virginia revealed 16,151 cavities exclusive of those containing fillings. Under-developed jaws and irregular teeth were surprisingly prevalent. 5,935 children examined showed these defects in 1,759 cases. There is nothing in our national life which is more pressing for attention or more important from the standpoint of public health than attention to this matter. The only effective way to attack the problem is through the diet of the expectant mother and of the infant and young child. This must be constituted better than is now the case.

350. **Significance of the Absence of Rickets in the West of Ireland.**—Of more than ordinary interest in connection with the problem of the cause of rickets is the immunity of the inhabitants of the West of Ireland (27) and of the Island of Lewis in the Hebrides (28). In the former place much land is unsuitable for agriculture and cattle and sheep raising are highly important industries. In fact there are few places in the world where the number of cattle in proportion to the population is greater than in Ireland. So far as the author's investigations have gone, everything points to the conclusion that wherever a region is hilly and unfit for agriculture, or where the soil is thin or poor and suited only for the grazing animals, fine physical development is characteristic of the people, and rickets is unknown or rare among the children. Where agriculture thrives and the growing of cereal grains and tubers is the most profitable form of agriculture, physical deterioration as shown by stunted growth, physical inferiority and defective development and caries of the teeth are likely to characterize the people both of

the rural districts and of the cities, but especially the latter, because their diet is likely to be derived in larger proportion from cereal grains, tubers and muscle meats.

351. **Significance of the Conditions in the Island of Lewis in Interpreting the Cause of Rickets.**—The Island of Lewis in the Hebrides is of very great interest in illustrating the greater importance of nutrition than of hygienic factors, in promoting health, in reducing the infant mortality and in preventing skeletal defects. It has already been pointed out that the natives of this island subsist on a diet consisting in great measure of cod's heads stuffed with cod livers, milk, fish, turnips, oat meal and potatoes, and that their diet is in great measure a carnivorous one, supplemented with small additions of cereal, tuber and root vegetables. They live under the worst conceivable hygienic conditions, with a filthy byre in one end of the dwelling, with no window or only a fixed one and with a peat fire constantly burning, the smoke of which can escape only through the thatched roof and through the open door. The babies are taken out of doors only for a few minutes at a time in bright weather, are deprived of sunlight and breathe an atmosphere sufficiently smoky to make inflamed eyes the rule, yet they remain practically free from rickets. The death rate of infants in the island has not infrequently fallen as low as any place in the British Isles. The influence which counteracts the bad hygienic conditions is the universal practice of breast-feeding, and by mothers whose diet, although unattractive to the palate of the average European or American, is, when evaluated on the basis of its biological value as shown by experiment, a highly satisfactory one. Such illustrations as the foregoing are very convincing evidence that the diet is the factor of primary importance in the etiology of rickets, and this belief is fully established by the experimental production of rickets and related skeletal defects in animals, when the diet was the sole cause to which the abnormalities of the bones could be attributed.

Several observers have recently reported the successful treatment of rickets by radiation with the rays from a mercury vapor lamp (very short rays), and with sunlight (29). It is necessary, therefore, that any discussion of the etiology of rickets, to be convincing, must satisfactorily account for the tendency for rickets to heal under such treatment. We have now an observation of extraordinary interest which is suggestive of the nature of the "cure" which is effected by light treatment. Further

studies will be necessary before a conclusive statement can be made relative to this matter, but the observation in question helps to clarify our views on this seemingly conflicting evidence concerning the importance of light as a means of preventing rickets.

352. **A Method for Demonstrating the Anti-rachitic Effect of Cod Liver Oil.**—It has already been described how, by appropriately planned diets it is possible to prepare young rats so that there is no calcium phosphate deposited in the zone of primary calcification of the bones, and that when this is brought about by deficiency of phosphorus, of fat-soluble A and anti-rachitic substance, together with a moderate excess over the optimal of calcium in the diet, the administration of cod liver oil during a period of a few days leads to the deposition of a fine line of calcium salts across the uncalcified region in the epiphysis of the bone. This sudden calcification is due to the effect of the organic nutritive substance which is abundant in cod liver oil, but essentially lacking in many of our common foods. It was reasoned by Shipley, Park, Simmonds and McCollum (30), that if by some means a disintegration of body protoplasm could be suddenly brought about, this might result in the liberation into the body fluids, from the destroyed protoplasm, the organic factors, calcium and phosphorus, and might make possible a deposition of calcium phosphate such as is seen in healing rickets. It seemed probable that a period of fasting would bring about a sufficient demand upon the body structures to bring about this result. A trial showed that this result is obtained.

353. **A Period of Fasting May Initiate the Healing of the Lesion of Rickets.**—When a young rat is placed for thirty days or thereabouts upon a diet such as has been described above for the purpose of preparing it for a demonstration of the therapeutic value of cod liver oil in the treatment of rickets, and is by such a dietary regimen brought to a condition in which the zone of primary calcification is free from lime salts, it will, we may suppose, respond to illumination, with the initiation of healing processes, as well as to cod liver oil therapy. If now, we permit such an animal to fast for a period of five days, and thereby force it to draw heavily upon certain tissues for food for others whose functioning is most essential, it has been shown that healing of the rachitic lesion takes place in essentially the same manner as from the administration of cod liver oil.

This seems to suggest a possible explanation for the good results observed in the treatment of human rickets by excessive illumination with sunlight or with highly penetrating rays. It seems probable that under such stimulating treatment, tissue destruction may be accelerated, and that the effect is to liberate thereby the substances which exert an anti-rachitic effect. Provisionally it seems warrantable to adopt as a working hypothesis for further investigation the view that highly penetrating rays produce visible effects comparable to a period of fasting, and give the impression that rickets is healing, but under circumstances where the actual cause of the disease has not been removed. This is only palliative therapy unless the nutritional situation is at the same time improved. It may be, of course, that the healing of rickets following starvation is due to the restoration of a normal salt balance in the body in which anabolic processes are brought to a very low level (48).

354. **Parallelism Between Increase in Incidence of Rickets and of Decayed Teeth.**—Since the incidence and severity of rickets have markedly increased in many places within recent times, and essentially parallel with it there has been a marked deterioration of the teeth, associated with underdevelopment of the jaws, and an increased tendency to general physical inferiority, we must look to some change or changes in living conditions which have brought about these results. On investigation we find that the pastoral peoples of Asia, Arabia, Northern Africa and Abyssinia are essentially free from the disease. This would be attributed by many to the "natural" conditions of living. England and Scotland have a high incidence of the disease, yet localities are found in both countries where the condition is rare or unknown. Ireland, the climate of which differs but insignificantly from certain other places where rickets is common, contains districts where it is unknown. The dampness of western Ireland is so great as to interfere seriously with the curing of forage crops for hay, yet the lack of sunlight does not promote rickets in the children, nor does the "black house" of the Hebrides, an extreme condition of lack of illumination and ventilation, cause the disease. It can be produced in animals under conditions in which all factors other than diet are eliminated, and in an animal, the rat, which is nocturnal in habits, and ordinarily lives under conditions of extreme filthiness, darkness and bad air without showing the least deviation from the normal in the structure of its bones. We must look, therefore, to our methods

of feeding pregnant mothers, lactating mothers, and infants and children, if we are to accomplish our purpose of eradicating this disease which stands first in importance in causing physical inferiority of the human race in Europe and America. We have in rickets another incrimination of the milled cereal, tuber and muscle meat type of diet. The progress in specialization in the direction of limiting the food supply largely to these classes of articles, is synchronous with the increase in the occurrence of rickets. Wrong dietary habits are the cause of rickets, and also of faulty tooth development, and of vulnerability of the teeth, which now is causing so much alarm.

355. **Effect of Light on Rickets.**—Several observers have recently reported the successful treatment of rickets in children by radiation with ultra-violet rays derived from the mercury vapor lamp, with X-rays and also with sunlight. It is necessary, therefore, that any discussion of the etiology of rickets, to be convincing, must satisfactorily account for the tendency for rickets to heal under such treatment. The work of several observers should be noted in this connection.

In 1904 Buchholz (31) reported the recovery of sixteen children suffering from rickets, on treatment with the rays of the "Glühlicht." The nature of the light was not described. As early as 1890 Palm (32) became convinced as the result of a noteworthy topographical study of the incidence of rickets, that the disease was rare or absent from regions receiving much sunlight, and progressively more common in others where the amount of sunlight was less abundant. He pointed out the desirability of accurate observations on the chemical activity of the sunlight of large cities, and recommended the use of sun baths and the removal of children suffering from rickets as early as possible to localities where sunshine abounds. In 1912 Raczynski (33) again correlated the relationship which exists between the incidence of rickets and lack of sunlight. He pointed out that the curve representing the number of cases admitted to the hospital began to rise sharply in January, reached a maximum in May and fell rapidly in June.

Raczynski reported an experiment with two puppies born of the same mother in May. One was kept in the sunlight from morning to evening, while the other was kept in total darkness. Both puppies were nursed exclusively by the mother. At the end of six weeks the two were killed for examination. It was found that the one which had lived in the light was normal

whereas the one kept in darkness had but poorly assimilated mineral salts necessary for the formation of a skeleton.

The use of the X-ray in tracing the development of the healing process in rickets in children has made possible more definite and accurate observations on the effect of therapeutic agents in the treatment of the disease. Fraenkel and Lorey (34) in 1910 published an atlas devoted to rickets, in which they reproduced X-ray pictures of the bones of rachitic children in all stages of healing and relapse. Phemister (35), in America, has used this method for the study of the effects of phosphorus on growth and ossification. With this aid Huldschinsky (36) studied many cases of rickets in children as they were effected by the ultra-violet ray. He found that under the influence of this type of radiation there was a deposition of calcium salts in the ends of the long bones which was observable in radiographs. Control children who were not treated with the rays showed no improvement.

In 1919 Winkler (37) reported very spectacular results in the treatment of rickets with the X-ray. Putzig (37) in the same year corroborated the findings of Huldschinsky as did also Karger (38) and Riedel (39). In 1921 further confirmation of the observations of Huldschinsky have appeared in the work of Sachs (40), Erlacher (41), Mengert (42) and Hess (43). Hess' views regarding the curative effects of radiant energy on children suffering from rickets, and based on his own observations, led him to assert in 1920 (44) that the violet ray was not effective in the treatment of rickets. He further stated in connection with a discussion of the value of sunlight as a preventive measure against rickets: "But the fact that rickets is exceptional in the Arctic regions where there is lack of sunlight for the greater part of the year is a strong argument against its predominant influence." Even Glisson in 1650 (8) expressed the view that moist, foggy climates were an etiological factor in the production of rickets. Since the appearance of the work of the German investigators noted above Hess (44) has reported new experiments which are fully in accord with the latter in supporting the view that ultra-violet light and sunlight are very effective in the treatment of the disease. In 1921 Hess and Unger (44) reported their demonstration by means of the X-ray, that sunlight alone possesses the same curative action as does the ultraviolet ray in human rickets. They exposed rachitic infants for periods of one-half hour to several hours daily whenever sunlight was

available. Different parts of the body were in turn subjected to the action of the rays. Under this treatment calcification of the cartilage-shaft junctions of the bones occurred.

Thus far all investigations relating to the curative effects of sunlight or of ultraviolet rays in rickets had been made on human subjects and all the evidence regarding their effects had been furnished by radiographs. Park, Powers, Shipley, Simmonds and McCollum (45) have recently carried out experiments with rats which were fed a diet which had previously been shown to induce rickets within a few weeks. Two groups of animals were employed. These were fed the same diet, and one group was kept in a northeast room in which there was no direct illumination except through glass and the light was always subdued. The other group was kept in direct sunlight in summer for varying periods. Individuals were given the sun treatment for 62-67 days, and the average period of exposure was four hours daily.

The control animals which were kept in a room with little light, all developed severe rickets as shown by autopsy and histological examination of the bones. They also showed the typical deformities described earlier in this chapter. The illuminated animals on the other hand, while they did not grow in a satisfactory manner, did increase in weight to a certain extent, and *none showed any signs of rickets.* This was confirmed by careful autopsies and by histological examination of sections of the bones.

The diet employed in this experiment consisted of wheat 33 per cent, maize 33 per cent, gelatin 15 per cent, wheat gluten 15 per cent, sodium chlorid 1.0 per cent and calcium carbonate 3.0 per cent. The diet was of good quality in respect to the content and quality of its protein. It contained about twice the optimal content of calcium; less than the optimal content of phosphorus and was very poor in fat-soluble A. Any diet so constituted will, as we have previously shown, cause the development of a condition of the bones which is anatomically indistinguishable from that seen in rickets of human beings.

The marked improvement in the rats exposed to sunlight over those which were not, affords convincing evidence that the good effect of the illumination was not limited to the bones, but had a profound influence on all the cells of the body. Sunlight is in this respect comparable with cod liver oil, which, when added to the diet employed in these experiments, not only makes the

bones essentially normal in structure, but also makes the appearance of the animals receiving it greatly superior to control animals on the same diet without the oil.

These results have a wide biological significance. Cod liver oil contains and sunlight embodies something which is essential for optimal cellular functioning. Either cod liver oil or light, when made available to an animal previously deprived of either, enables the organism to put into operation defense mechanisms or adaptations which it could otherwise not avail itself of. Neither cod liver oil nor light corrects the defects of the diet as respects the faulty relation of calcium and phosphorus, for the oil does not contain either of these elements. It is this faulty content of the diet with respect to calcium and to phosphorus which plays the most significant rôle in predisposing the animal to the development of the rachitic syndrome. Either cod liver oil or light serves, however, to make the cells function more satisfactorily under these unfavorable conditions than they otherwise could do. They raise the potential of cellular activity so as to secure a most efficient utilization of the calcium and phosphorus available for bone formation. Without one or the other of these agencies acting, the animals would develop rickets on this diet, but under their influence bone growth is essentially normal. Under their influence the animals do not suffer from general physical debility as they otherwise would. Sunlight enabled the animals to adapt themselves not only to a shortage of a vitamin (fat-soluble A) but also to the unfavorable relationship between the calcium and phosphorus in the diet.

It is apparent from these results that, within certain limits, diets which are deficient in some degree with respect to certain factors, when the body receives only subdued light or is kept in darkness, may suffice in much greater degree to maintain nutrition and promote well-being in the same species under circumstances where a good supply of sunlight is available. It seems to be definitely proven that a certain amount of sunlight is beneficial to physiological well-being. The possibility is also suggested that a diet which supplies the optimal amounts of certain dietary factors for an animal living in darkness or semi-darkness, may furnish excessive amounts for an individual which is bathed in light. This question is deserving of further inquiry.

Since cod liver oil is able to act as a substitute for active light in its effect on certain of the processes of growth and metabolism, it becomes necessary to think of it (and probably certain

other foods as well) as being able to compensate for deprivation of light. The mechanism which is operative between light and certain foods is reciprocal, in that they are interchangeable. It is conceivable that the extent to which the body is irradiated by sunlight may determine in an important degree the amounts of certain dietary essentials which will suffice for the maintenance of satisfactory physiological well-being.

It may well be significant that people who live in the far north and receive little sunlight, take regularly in their food large amounts of fish oils and other fats. The same is true of Arctic animals of carnivorous dietary habits. This element in their food must, it appears, compensate for the lack of illumination, for rickets is very rare in that part of the world. On the other hand, rickets is also rare in the warmer parts of the world, and this may now in great measure be correlated with the amount of sunlight which is received. We may expect severe rickets to become common in the Arctic regions should the type of diet which is common in lower latitudes of America supplant the primitive diet. There appears, as already mentioned earlier in this chapter, to be evidence that rickets is already appearing among children in northern Alaska. The infants in the "black house" of the Hebrides are protected against skeletal defects through the consumption by their mothers of cod heads stuffed with minced cod livers.

It appears, therefore, that Nature has provided a substitute for light in an organic substance or substances contained in certain foods, and that the function of these may be in some way associated with the provision of some form of radiant energy, produced, it may be, through oxidation of compounds of unique character. This view, resting as it does, on a sound experimental basis, opens a new and attractive field for investigation. It introduces into nutrition problems factors which the physicist must be called upon to help solve, and must stimulate profound inquiry into the therapeutic possibilities of purely physical agencies which have hitherto been employed in a haphazard manner and based on empirical reasoning.

It should be emphasized, in view of what has just been said, about the possibility of affording a measure of protection for an animal restricted to a diet which is deficient in certain respects, by providing it with a liberal supply of a particular vitamin (calcium-depositing substance), that this does not afford a justification for relaxing our insistence upon the wisdom of

taking regularly a diet which is just as nearly of optimal composition as possible. When the diet is defective in any respect, the enhancement of the food with respect to any other factor or factors will make the animal able to appear better nourished than it otherwise would, but the defect is certain to leave its mark somewhere in the life history of the individual or its progeny.

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FIG. 16.—Illustrates the appearance of the exterior of the thorax of a normal and of a rachitic rat. The animals were the same age. The normal one on the left exhibits the perfection of form in this species. The rickety rat was small, round shouldered, and had the typical "pigeon breast" seen in severe cases of rickets in children. The bending inward of the ribs resulted in a flattening and deformity of the thorax, and the formation of a groove along the line of insertion of the diaphragm.

Fig. 17.—Illustrates the appearance of the inside of the thorax of a normal rat and also one suffering from rickets. Note the smooth and symmetrical form of the normal animal on the left. On the right the rickety rat is seen to have great deformity of the thorax. The shoulders are rounded and the breast bone misshapen. There are large knobs on the ribs due to spontaneous fracture and attempt at healing. The junctions of the ribs with the cartilages are enlarged, and the ribs are bent inward at their ventral extremity. The beaded condition of these is the analogue of the "rachitic rosary" seen in children.

CHAPTER XV

THE NURSING MOTHER AS A FACTOR OF SAFETY IN THE NUTRITION OF THE SUCKLING

355. **New-Born Young Dependent on Milk.**—It is a remarkable fact that for a time after birth every mammal is incapable of taking the type of diet which suffices for the maintenance of normal nutrition in the adult. It must have milk for a certain period. The duration of dependency on a milk diet is not the same for different species. Among all the mammals the young of the guinea pig appears to have the shortest period of dependence upon the mother. It is born in a very advanced state of maturity and can eat grass or succulent vegetables during the first or second day of post-natal life. The young rat may safely be weaned at the age of twenty-five days, provided the diet of the mother during the time of nursing is satisfactory, and provided the young are put as soon as weaned, upon a diet of good quality. If the mother's diet has been faulty in any respect it may be necessary to prolong the nursing period to thirty to fifty days before the young reach a state of independence. The young pig (swine) is able to eat at six to eight weeks fairly liberally of the normal diet of forage plants and cereals or roots. The human infant must live during the first year of life largely on a milk diet, and cannot thrive without a fairly liberal supply of milk during a considerable part of the entire period of growth. Even eggs cannot entirely replace milk during any part of the nursing period. It is of great importance that we should understand the relationship between the character of the diet of the lactating female and the quality of the milk secreted. Our knowledge of this phase of nutrition has been greatly enhanced during the last few years, and the general principles are now well understood.

356. **Effect of Faulty Diet on the Capacity of the Lactating Female to Produce Normal Milk.**—In order to gain information concerning the relation between the character of the diet of the mother and the nutritive quality of her milk, McCollum and

Simmonds (1) carried out a series of experiments with lactating rats, whose diets were faulty in known respects. They observed the effect on the growth of the young nursed by mothers receiving a highly satisfactory diet until the completion of their term of pregnancy. As soon as the young were born the litters were in all cases reduced to four in order that the nutritive undertaking of the mother should be in no case burdensome. The mother was at once placed upon a diet which would not induce any growth in a young rat separated at weaning time from the mother. The food of the mothers in the course of various experiments was made faulty in different respects. The faults included all the recognized factors which contribute to making a diet satisfactory, but the number of deficiencies in any single diet varied from one to three.

In one case a mother was fed upon a diet of purified protein, carbohydrate and a salt mixture supplemented with an alcoholic extract of wheat germ to furnish the factor, water-soluble B. This diet contained everything necessary for the nutrition of a young rat during growth, except fat-soluble A. The problem was to find whether the mother could, through the agency of the mammary gland, synthesize this substance from some other component of her diet. Experience has shown that the young animal after weaning cannot, for its own preservation, produce the fat-soluble A from other complexes in its food. The results of these experiments indicated clearly that the quantity of fat-soluble A in the milk of the mother confined to this deficient food was distinctly below the optimum, or below the average content of milks. The milk secreted under the circumstances did not furnish a sufficient amount of this substance to promote growth in the young at the maximum rate.

357. **Mammary Gland Has No Power to Synthesize a Vitamin.**—When McCollum and Davis first observed the necessity in the diet for growth of something which could be furnished by certain fats but not by others or not by non-lipin components of the diet, they were impressed by the experiments reported by Osborne and Mendel (2). The latter appeared to have demonstrated that a pregnant female could cause the development of normal young, and thereafter secrete milk containing everything necessary for their normal nutrition, while herself confined to a diet which lacked, so far as could be seen, not only the amino-acid lysin, but likewise any source of the dietary factor now designated as fat-soluble A. The experimental diet consisted

of gliadin, protein-free milk, starch and lard. Osborne and Mendel's experiment in reproduction on this food mixture seemed to prove that the synthesis of vitamins by the mammary gland was possible. It appeared, therefore, that they could be produced by the mother for the preservation of the species, but not by the young for their own preservation. This assumption was at that time believed to be supported by satisfactory experimental data (3). Later studies by McCollum and Simmonds have clearly demonstrated that there can be no adequate nutrition of the young while nursing a mother whose diet is deficient in fat-soluble A, or any other substance which the young rat requires for its nutrition in after-weaning periods.

It has been shown by Osborne and Mendel (4) that body fat of beef cattle contains a small amount of fat-soluble A. It seems certain that the body fats of any animal fed for a time a diet rich in this substance will serve as a reserve supply of this factor, which the mother can draw upon and secrete into the milk. In other experiments of McCollum and Simmonds definite evidence was secured which *proved that fat-soluble A is not present in the milk unless it is furnished in the food of the lactating animal.* The presence of some fat-soluble A in the tissues of the mother makes it especially difficult to obtain milk entirely free from this substance.

Through similar experiments with diets which contain fat-soluble A but not water-soluble B, evidence was also secured that for a time the mother is able to secure this dietary factor from her reserve supply, *but none of the growth curves indicated that this substance is present in adequate amounts in the milk when the diet of the mother is lacking therein. It seems certain that neither of these dietary essentials is present in abundance in milk unless the diet of the lactating animal serves as the source.*

358. **Tendency for the Lactating Mother to Sacrifice Her Tissues to Maintain the Normal Composition of Her Milk.**—It is hardly to be expected that the quality of the milk should be maintained unimpaired when the nutrition of the lactating mother falls far below the normal for any very extended period. Indeed, many observations are recorded which show that the milk secreted by poorly nourished women is of low nutritive value. There is, nevertheless, some tendency for the mother to sacrifice herself in order to produce milk for the maintenance of her offspring. Ducaisne (5) observed that during the siege

of Paris, young and vigorous women were able to produce milk enough to maintain their infants. In some instances the lactating mothers, while partially fasting, actually increased their weight.

During the great war the state of malnutrition among the children of many parts of Europe caused great concern. Chemical investigations of the composition of human milks produced by women not able to furnish proper nourishment for their babies were reported by Mömm and Kraemer (6). They observed in the fat content no appreciable deviation from the normal. Kaupe, a pediatrist of Bonn (7), found in his clinic that the milk secreted by women during the war was sufficient in *amount* to induce during the first few weeks of life satisfactory nutrition. The children did not, however, gain in weight as they should. The average volume of milk produced by these mothers during the eleventh to the thirteenth day after their infants were born, he ascertained to be 440 c.c. Weeks or even months frequently passed before the children regained the weight which they had lost immediately following birth, when there was no evidence of disease. Kaupe was led to the conclusion that artificial feeding should be resorted to in order to save babies failing to develop satisfactorily on breast milk. He was unable to explain the nature of the changes which rendered the breast milk inadequate for the nutrition of the infants, and was inclined to attribute to psychic influences the deterioration in its nutritive value.

359. **Chemical Composition of the Milk of Pellagrous Women.**—Voegtlin and Harris (8) state that pellagra sometimes occurs in breast-fed infants. They made an investigation of the milk of pellagrous women and reported that: "The volume may be normal or reduced, depending somewhat on the general nutritional state and food consumption of the patient. Very severe cases often secrete only 100 to 300 c.c. or less of milk per day, whereas we have records of milder cases which yielded approximately one half to one liter. Lactose, fat, protein-nitrogen, and total solids were found to fall within the normal limits, but considerably below the normal average. The total ash and the phosphate content were normal. A slight reduction in the quantity of calcium, magnesium and potassium was noted, whereas chlorids and sodium were present in larger amounts. The character of the diet had no influence on the percentage composition of the milk, with the exception that a change from a vegetable to a mixed diet was accompanied by a marked increase in the total non-protein nitrogen. The conclusion to be drawn

from these observations is that well marked cases of pellagra yield a milk, which, as far as its composition with respect to the known milk constituents is concerned, does not show a sufficient deviation from the normal to account for the disease in nursing infants."

360. **The Effects of Under-Feeding on the Lactating Cow and the Composition of Her Milk.**—Eccles and Palmer (9) have conducted a very thorough experimental study of the influence on milk production of the under-feeding of cows. They have examined the composition of milk produced by cows whose rations were, from a qualitative standpoint, suitable biologically, but inadequate in amount. Their results show that cows were able, during the early part of the lactation period, to maintain the milk flow undiminished for forty days, during which they received but 75 per cent of the quantity of food sufficient for their requirements. Under such conditions of nutrition there were no pronounced changes in the composition of the milk. During the latter part of the lactation period there was, however, as the result of underfeeding, some falling off in milk secretion.

361. **Deficiency in the Milk of Women Suffering from Beri-Beri.**—Interesting evidence on the effect of an inadequate diet in lowering the nutritive value of the milk secreted, is afforded by the studies of Andrews (10). It is well known that infants, who subsist upon the milk of mothers suffering from beri-beri resulting from a simple and monotonous diet of rice, fish and very small amounts of other foods, frequently develop the disease during the first few months of life. This is due, in such cases, to a lack in the milk of a sufficient quantity of the anti-neuritic substance, water-soluble B. Andrews fed the milk of women suffering from beri-beri to young pups and found that they soon lost the use of the hind legs and showed other evidences of beri-beri.

It will be seen, therefore, that although faulty diet in a lactating female will not ordinarily modify in respect to the ordinary components for which the chemist has methods for analysis the composition of the milk which she secretes, it may very easily lower the nutritive value of the milk to such an extent as to render it unfit food for an infant. McCollum and Simmonds (1) have established experimental conditions which serve to illustrate how far faults of various kinds and of different degrees in the diet of mother rats influence the rate of growth in their young.

362. **A Cereal Diet Is Not Satisfactory for the Formation**

of Normal Milk.—It has been pointed out that young animals do not grow when confined to a single cereal or other seed or mixture of seeds, for the reason that these are all deficient in the inorganic elements, calcium, phosphorus, sodium and chlorin, and are too poor in fat-soluble A to support normal nutrition. Likewise the proteins are too poor in quality to maintain satisfactory growth, unless fed at higher planes of intake than can be secured with cereal mixtures. McCollum and Simmonds (1) have studied the extent to which the mother rat, confined to a single seed as the sole source of nutriment, is able to secrete milk of a character satisfactory for the promotion of growth in her young. Chart 9 shows the effects of such diets on the growth of the nursing young.

363. **Failure of the Lactating Rat to Induce Growth in Her Young While Confined to a Diet of Rolled Oats.**—The curves of rat 211 and her litter of four young (Chart 9) illustrate the remarkable growth which the mother rat is capable of inducing in her offspring when the diet is highly satisfactory. While so doing she is also able to increase her own weight very appreciably. In marked contrast to this "normal" accomplishment, stands the failure of rat 738 to induce in her young growth at more than one-third the optimal rate, when restricted to rolled oats as her sole food supply (1). The drop in the curve of the weight record of the young at the fortieth day was the result of the death of the young at short intervals. The mother lost weight steadily, a fact which indicated the sacrificing of her own tissues for the preservation of her young. Rolled oats, like other seeds of plants, requires improvement in respect to at least four dietary factors before it becomes a complete food. If we regard as a distinct entity the organic substance which plays an important rôle in regulating the development of the bones, then there are five factors in which the oat kernel is deficient. This is true in some degree of all the other cereal grains and legume seeds. These and similar records of female rats confined to a single cereal grain as their only food, show clearly that the deficiencies in these grains are sufficiently serious to interfere with normal milk production.

364. **Effect on the Quality of the Milk of Supplementing the Oat Kernel.**—A rat (1) whose diet consisted of rolled oats supplemented with fat-soluble A in the form of butter fat, induced growth in her litter of four at a rate somewhat greater than she could have done had she eaten rolled oats alone. On this food

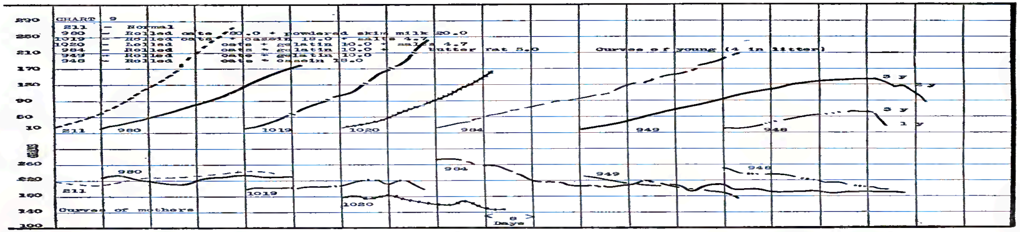

CHART 9.—The curves at the top of this chart show the rate of growth of litters of four young each, when they were nursed by mothers taking the diets listed. No. 211 is an excellent diet containing a liberal amount of dried milk. On this the mother is able to induce rapid growth in her young.

Lots 980, 1019 and 1020 were given rolled oats and a protein supplement, either gelatin or casein, together with a mineral salt addition. Lots 984, 949, and 948 did not receive the supplementary salt additions. The inferiority of their young as contrasted with the first named group is very marked. Lot 984 was given a supplementary supply of fat-soluble A over that which was contained in the seeds. This prevented the early failure of the young as happened in Lots 948 and 949 which were not given an additional supply of this substance over what was furnished by rolled oats. These curves show clearly that the quality of the mother's milk is profoundly influenced by the character of her diet. If she is selectively fasted for mineral elements, fat-soluble A, water-soluble B, or water-soluble C, or if the proteins of her diet are not of good quality her milk is deficient in the substances which are wanting, relatively, in her diet. It is of the utmost importance that the diet of the nursing mother should be of very excellent quality with respect to all its parts.

The curves at the bottom of the chart are also of great interest. Note that those mothers which were fed rolled oats supplemented with a protein and a salt mixture were able to sustain their body weight much better than could those which were fed oats and a protein or oats, protein and butter fat. The draft upon the vitality of the mother while nursing young will be greatly relieved by making her diet highly satisfactory. Note that Lots 948, 949 and 984 lost weight much more rapidly than did those mothers whose diets were better constituted for the promotion of growth in their young.

mixture she was able to keep them alive for a somewhat longer period. The first one died on the 57th day and the remaining ones followed in rapid succession. This mother lost considerable weight up to the time when the young began to eat of the oat and butter fat diet. Young rats, after removal from the mother, cannot grow on this diet.

A mother rat was fed a diet of rolled oats to which was added an inorganic salt mixture so made up as to correct the mineral deficiencies of the oat kernel. Her diet still lacked fat-soluble A and the anti-rachitic substance and its proteins were below the optimum both in quality and quantity. With this food her milk was distinctly better in quality than she could have secreted had she been restricted to either oats alone or to oats and butter fat or to oats supplemented with purified protein. From these results it is apparent that for milk production the first limiting factor in the oat kernel is the same as for growth in the young. That limiting factor is the inorganic content of the food supply.

365. **Inorganic Content of the Diet Is Very Important for the Secretion of Normal Milk.**—The importance of having the inorganic content of the diet properly constituted is shown especially well in the histories of the mothers 983 and 1978 (1). The former was fed rolled oats supplemented with both fat-soluble A (supplied as butter fat), and purified protein in the form of casein. Even with these two additions she was able to induce in her young less than half the normal growth. The young began to die at the age of 45 days and succumbed in rapid succession. Rat 1978, on the other hand, whose diet consisted of rolled oats supplemented with a suitable salt mixture and butter fat, was able to produce milk which induced growth in her litter at about two-thirds the maximum rate observed in the case of well fed mothers. The improvement of the milk by the inclusion of fat-soluble A in the diet was very apparent, since the young were able to live beyond the period of the sixty days covered by the experiment. *These observations support the view that fat-soluble A cannot be synthesized by the mammary gland.*

The experience of rat 1019, Chart 9, whose diet consisted of rolled oats supplemented with purified protein and a suitable salt mixture, showed that the mother was able to induce in her young nearly normal growth during a period of thirty days, although her diet was very poor in fat-soluble A. It should be borne in mind that the seeds, because they contain a small

proportion of cellular structures in addition to their reserve food package in the endosperm, contain but a small and inadequate amount of fat-soluble A. The mother is able, when her diet of oats is corrected with respect to two factors, protein and salts, to concentrate in the milk the small amount of fat-soluble A in her food, and perhaps to supplement this in some degree with the reserve in her own fatty tissues. In this way she is able to bring the young to a state of relative independence while she herself is subsisting on a food supply not capable of inducing any growth whatever in the young. There is abundant experimental proof that when the protein and the inorganic contents of the diet are satisfactory, animals can maintain themselves for a long period on a supply of fat-soluble A too small to prevent xerophthalmia in animals whose diets are more poorly constituted in respect to other factors.

366. **Milk Secretion Governed by Same Laws as the Nutrition of the Growing Young.**—These records of nursing mothers and their young make it apparent that the former are limited in the utilization of food for milk production, in the same manner as the growing young are limited in the utilization of food for the construction during growth of new tissues. The mother is to no small degree, however, a factor of safety for the young. It should be remembered that the young rat cannot grow at all when after weaning it is confined to the oat kernel alone or to this cereal supplemented with protein, fat-soluble A, or a salt mixture alone, or on a diet in which oats are supplemented with both protein and fat-soluble A. In order that it may grow even very slowly it is essential that both a salt mixture and fat-soluble A be added to the oat. It is not possible for it to grow normally on such a mixture unless protein is also supplied.

367. **The Nursing Mother as a Factor of Safety for Her Young.**—In the records of the mothers on modified oat diets, the young in certain cases continued to grow after the 25th day, at which age they may be safely weaned if supplied with a good food mixture, and if their growth was optimal during the nursing period. This fact is evidence that even after the young are able to eat of the deficient diet from which the mother has produced milk suitable only for subnormal growth, and on which they would be unable to grow at all, they are capable of developing in a fairly satisfactory manner for a time if they are supplied with a small contribution of their mother's milk to supplement the deficient cereal diet. There can be no doubt that they were

still receiving a supplementary milk supply from the mother and that this served to enhance the incompletely supplemented oat diets available. Under adverse circumstances, therefore, a young animal restricted to an inadequate diet can be safely tided over a considerable interval, during which it would succumb were it not for the peculiar relation between the mammary gland and the blood, through which it secretes into the milk certain nutrient principles in amounts larger than those present in the food of the lactating female.

The inorganic content of all the plant seeds is the limiting factor in preventing growth in young animals restricted to such a diet, and in determining the quality of the milk secreted by a female taking a seed diet. Although the young, after reaching a state of independence of the mother, cannot grow at all on a seed diet unless it is enhanced with respect to certain mineral elements, the mother is able to take such a diet without salt additions and to produce milk therefrom which is capable of inducing at a slow rate growth in the young. It is apparent that one of her most important relations to her dependent offspring lies in her capacity to provide for them more adequate nutrition than she herself may be able to secure. This applies with special force to the inorganic moiety of the milk she produces for them.

368. **Deficiencies of All the Cereals Are Comparable as Material for the Elaboration of Milk.**—The growth curves of the young of mothers, whose diets consisted of the oat kernel with and without purified food additions, likewise illustrate very well the results observed when similar experiments were conducted with the wheat or maize kernel. They emphasize the fact that, for milk production as well as for growth, the cereals and other seeds may be regarded as closely similar in their properties. It is rendered highly probable, therefore, that the same analogy in reference to value for milk production runs through the series of food-stuffs of this class. From chemical analyses we know that the seeds, tubers and fleshy roots contain inorganic elements in proportions and amounts which, in a general way, place them all in the same class. This is especially true with respect to their low content of calcium, sodium and chlorin, and in a lesser degree of phosphorus. We are, therefore, not to expect that any diet derived solely or nearly so from these classes of foods will prove very satisfactory for the production of milk of good growth-promoting power. The farther the diet falls short of the optimal for milk formation the greater the strain

placed upon the lactating organism, because of the tendency to self-sacrifice with respect especially to its inorganic reserves. Under such circumstances these would deviate from the optimal in the body fluids and tissues, and would cause deterioration of the maternal vitality. That such an occurrence is common there can be no room for doubt.

369. **Importance of the "Protective Foods" in the Nutrition of the Nursing Mother.**—It should be reiterated that there are two classes of food-stuffs, of peculiar value in human and animal nutrition. These tend strongly to correct the deficiencies in a cereal, legume seed, tuber and fleshy root diet, or one in which in addition to these muscle meats are included. These are milk and the leafy vegetables (11). These, the protective foods, should always play a prominent rôle in the nutrition of man. Eggs and the glandular organs of animals such as liver, kidney, etc., serve to correct partially the deficiencies of the type of diet derived solely or nearly so from vegetable foods functioning as storage tissues, but they cannot take the place of milk and the leafy vegetables because they are too poor in calcium. The observation of Steenbock that certain edible roots contain considerable amounts of fat-soluble A does not alter in a practical way the supplementary relationship between the two classes of foods discussed, for the protein and inorganic factors are not much improved by making combinations of any foods of the type of storage tissues.

370. **Extent of Self-Sacrifice of the Lactating Mother for Her Young.**—The tendency of the lactating female to persist in secreting milk, even though deficient in one or more respects as a food for the suckling because of faults in her diet, is truly remarkable. Babcock (12) described experiments in which he deprived cows of common salt during lactation. The animals were not entirely deprived of salt since they were fed on ordinary farm products, all of which contain salt, but they were not given any supplementary supply, as is the custom among farmers. In Wisconsin an ordinary grain and roughage ration does not furnish even approximately enough sodium chlorid. Deer, living on grass and the leaves of shrubs, develop such an appetite for salt, that, although they are by nature very shy, they will brave any danger to visit their accustomed salt licks. In Babcock's experiments the period of deprivation of salt varied from two to fifteen months. Some of the animals died from lack of salt and others were saved from death only by its administration.

In no instance was there any noticeable decrease in the yield of milk until a short time before the cows began to fail rapidly. The fat content of the milk from cows suffering from partial salt starvation was somewhat higher than that of the milk of the control group. Long before the cows showed any sign of injury from lack of salt the milk became practically chlorin-free. This illustrates the fact that common foods do not necessarily furnish enough of certain elements to meet the needs of a lactating mother to enable her to secrete a milk of normal composition. This is true of calcium and probably of phosphorus.

371. **Effect of the Feed of the Cow on the Anti-scorbutic Properties of Her Milk.**—Hart, Steenbock and Ellis (13) experimented with the milk of cows which had been confined for a year or more to rations consisting of air-dried grains and forage plants and which had never, during these months, been allowed to eat any fresh or green food. The object of these investigators was to determine whether such milk had less anti-scorbutic value than milk derived from cows provided with fresh foods of vegetable origin. *Their results show clearly that the content of the anti-scorbutic substance in milk is dependent upon the diet.* Summer pasture milk is much richer in this nutritive factor than milk from cows fed upon dried feeds. It is of special interest to mention that they found that even when cows were restricted to a diet, which, because of drying, had little anti-scorbutic value, the mammary gland tended to concentrate a relatively large amount of this factor in the milk. Thus the milk from dry-fed cows protected guinea pigs from scurvy only when 75 c.c. was given daily, whereas about 50 c.c. were required of milk from cows on pasture. Here we have further evidence of the rôle of the lactating mother in elaborating a food for her offspring, which is of better quality than her own supply.

Dutcher and his coworkers (14) have conducted a considerable number of experiments with winter and with summer milks, which were secreted by cows kept on dry rations and on green food, respectively. Their data make it evident that 20 c.c. of summer milk were superior in anti-scorbutic potency to 60 c.c. of winter milk. Their results showed that when a cow passed from a green pasture ration to one of dry feed, her milk did not immediately undergo deterioration in respect to its anti-scorbutic value. Only after a period of five to eight weeks was there sufficient change in the quality of the milk to show its effects on guinea pigs. On ingesting fresh food, the milk immediately rose

in anti-scorbutic value. Such experiments as the ones just described illustrate the great importance of the character of the diet of the lactating mother and the great importance of the method of feeding cows to be used for the production of milk destined for infant feeding.

372. **Illustrations of the Gravity of Various Types of Faulty Diets on Quality of Milk.**—McCollum and Simmonds (15) have studied the effects on the rate of growth of young rats, of different types of deficiencies in the diet of the lactating mother. The results are shown in Tables XI, XIII and XV. In Table XV are shown the weights of litters of young containing different numbers and at various ages during the nursing period, as well as later after they became able to supplement the mother's milk with the diet on which she had nursed her young. These weights serve as normals for comparison with the weights of the young of other mothers whose diets were faulty in some respect. Table XIII shows the effects on the young of depriving the lactating mother of sufficient calcium.

Although the data in the tables are self-explanatory, a few cases of marked contrast may be mentioned. Rat 2153 had five young and was given a satisfactory diet while nursing. At fifteen days from birth their collective weight was 137 grams. Rat 2365 likewise had five young. She was fed a diet containing but 9 per cent of protein, two-thirds of which was derived from barley and one-third from navy beans. When the young were eighteen days old they weighed collectively but 70 grams. The protein moiety of this mother's diet was of rather poor quality and she was unable for this reason to secrete a satisfactory milk supply.

Rat 2767 on a normal diet of good quality had a litter of six young. At the age of nineteen days they weighed collectively 163 grams. On the other hand, rat 2785 on a diet too poor in calcium had six young, which at the age of twenty days weighed altogether but 73 grams. The tables afford a number of such contrasts in the state of development of the young where the mothers ate all their appetites called for of diets comparable in certain cases in composition to diets employed by people in the United States. It is a highly significant fact that a number of these diets were unsatisfactory for the proper nursing of young.

373. **Quality of Milk Falls Off Before Amount of Secretion Is Markedly Interfered with.**—The question will naturally arise in the mind of the reader as to whether the failure of the young

[Continued on page 352]

TABLE XI

Showing the Rate of Growth of Young Rats When the Diet of the Mother Is of Fairly Satisfactory to Good Quality.

No. of Experiment.	Wt. of Mother After Young Were Born. Grams.	Wt. of Mother 10 to 19 Days Later. Grams.	Wt. of Mother at End of Nursing.		No. of Young.	Weight of Young at Different Ages.					
			Day.	Grams.		Days.	Grams.	Days.	Grams.	Days.	Grams.
1236	142	... ...	40	146	7	16	133	30	286	40	544
2811	205	19th day... 225	28	215	10	19	225	28	387	..	...
2069 *	215	10th day... 232	22	205	4	10	100	22	197	..	...
2767	270	10th day... 275	29	270	6	19	163	29	330	..	...
2153 *	175	15th day... 182	28	192	5	15	137	28	277	..	...
2436	200	... ...	32	185	8	18	188	32	420	..	...

* The diets of lots 2069 and 2153 were less satisfactory than the others. On these two diets the animals in the second and succeeding generations became progressively stunted.

TABLE XII

Composition of Diets Used in Experiments Described in Table XI.

No. of Experiment.	Beefsteak Grams.	Wheat Grams	Maize Grams.	Rice Grams.	Oats Grams.	Peas Grams.	Navy Beans Grams.	Casein Grams.	Dextrin Grams.	Milk Powder* Grams.	Butter Fat Grams.	Wheat Flour † Grams.	Corn Meal ‡ Grams.	Cabbage § Grams.	$CaCO_3$ Grams.	NaCl. Grams.	KCl Grams.	Cod Liver Oil Grams.
1236. .	50.0								43.5		3.0				1.5	1.0	1.0	
2811. .		25.0	11.5	9.5	9.5	9.5	9.5	10.0		10.0	3.0				1.5	1.0		
2069. .	10.0			8.0	8.0	8.0	8.0					30.0	15.5	10.0	1.5	1.0		
2767. .		30.0	19.0	9.5	9.5	9.5	9.5	10.0							0.5	1.0		1.0
2153. .	10.0			9.5	9.5	9.5	9.5					30.0	19.5		1.5	1.0		
2436. .	10.0	30.0	19.0	9.5	8.5	8.5	8.5				3.0				1.5	1.0		

* Merrill-Soule Whole milk powder.
† Bolted wheat flour.
‡ Degerminated cornmeal.
§ Desiccated cabbage, subsequently steamed and dried.

TABLE XIII

SHOWING THE STUNTING EFFECT ON THE NURSING YOUNG OF DEFICIENCY OF CALCIUM IN THE DIET OF THE MOTHER.

No. of Experiment.	Wt. of Mother After Birth of Young. Grams.	Wt. of Mother 10 to 20 Days Later.		Wt. of Mother at End of Nursing.		No. of Young.	Weight of Young at Different Ages.					
		Days.	Grams.	Days.	Grams.		Days.	Grams.	Days.	Grams.	Days.	Grams.
2785 *	165	20	157	35	165	3	20	73	35	162	..	...
2733 †	150	13	150	34	151	4	13	48	34	151	61	184
2069 ‡	215	10	232	22	205	4	10	100	22	197	..	...
2732 §	155	18	160	45	150	6	18	90	34	210	54	247 (Five young)
2767 ‖	270	19	275	29	270	6	19	163	29	330	..	...
2782 ¶	182	14	160	30		8	19	109	30	172	39	210
2436 **	200	..	...	32	185	8	18	188	32	420	..	...

* Diet consisted of wheat, maize, rice, oats, peas, beans, casein, NaCl, butter fat and cod liver oil. (See p. 349.)
† 2733 Diet same as 2785 except that cod liver oil was the only fat added, and casein was substituted by beefsteak.
‡ Diet consisted of beefsteak, oats, peas, beans, rice, cabbage, wheat flour, corn meal, $CaCO_3$, and NaCl.
§ Diet similar to 2733 but with less cod liver oil. (See p. 349.)
‖ Diet closely similar to 2785, but contained 0.5 per cent of added $CaCO_3$. Note benefit to growth of young.
¶ Diet like 2785 except that casein was omitted. (See p. 349.)
** Diet similar in properties to the others used in these experiments but with the optimal amount of calcium carbonate added (1.5 per cent). Note the remarkable stimulating effect on the growth of the young.

TABLE XIV

COMPOSITION OF DIETS USED IN EXPERIMENTS DESCRIBED IN TABLE XIII.

No. of Experiment.	Beefsteak. Grams.	Wheat Grams.	Maize Grams.	Oats Grams.	Peas Grams.	Navy Beans Grams.	Rice Grams.	Casein Grams.	Cabbage* Grams.	Wheat Flour† Grams.	Corn Meal‡ Grams.	Butter Fat Grams.	Cod Liver Oil§ Grams.	$CaCO_3$ Grams.	NaCl Grams.	$NaHCO_3$ Grams.
2785		25.0	20.0	10.0	9.5	9.5	10.0	10.0				2.0	1.0		3.0	
2733	10.0	30.0	19.5	8.5	8.5	8.5	9.5						3.0		1.0	1.5
2069	10.0			8.0	8.0	8.0	8.0		10.0	30.0	15.5			1.5	1.0	
2732	10.0	30.0	19.5	9.5	9.5	8.5	9.5						1.0		1.0	1.5
2767		30.0	19.5	9.5	9.5	9.5	9.5	10.0					1.0	0.5	1.0	
2782		30.0	20.0	11.0	11.0	11.0	11.0					2.0	1.0		3.0	
2436	10.0	30.0	19.5	8.5	8.5	8.5	9.5					3.0		1.5	1.0	

* Cabbage desiccated, steamed and subsequently dried.
† Bolted wheat flour.
‡ Degerminated corn meal.
§ Norwegian cod liver oil employed in all experiments.

TABLE XV

SHOWING WEIGHT CHANGES OF FEMALE RATS AND THEIR YOUNG DURING THE NURSING PERIODS AS INFLUENCED BY THE CHARACTER OF THEIR DIET.

No. of Experiment.	Weight of Mother After Young Were Born.	Weight of Mother 10 to 18 Days Later.		Weight of Mother When Through Nursing.		Weight of Young at Different Ages.						No. of Young.	Generation on Diet.
	Grams.	Days.	Grams.	Days.	Grams.	Days.	Grams.	Days.	Grams.	Days.	Grams.		
2436 *	200	17	250	28	222	17	140	28	258	..	...	6	1st
"	257	11	277	25	265	11	185	25	200	..	...	4	2nd
"	182	..	...	30	180	16	132	30	305	..	...	6	3d
"	180	17	195	30	195	17	170	30	335	..	...	6	4th
2153 †	220	..	...	31	225	11	170	31	400	..	...	10	1st
"	175	15	182	28	192	15	137	23	208	28	277	5	1st
2069 ‡	200	27	172	35	177	12	115	27	243	35	342	7	1st
"	167	31	173	38	175	17	135	31	275	38	390	6	2nd
"	135	14	150	28	145	14	90	28	202	..	...	4	3d
2360 §	175	31	175	..	...	12	95	19	148	31	265	6	1st
"	142	22	152	33	154	14	120	27	225	33	350	7	2nd
"	115	30	128	37	132	..	...	30	209	37	262	7	3d

* Diet very good. It consisted of wheat, maize, oats, rice, peas, beans, beefsteak, NaCl, $CaCO_3$, and butter fat. Full formula is given on page 351. There was no deterioration observable in the 4th generation.

† The females of the 2nd generation never had any young. The diet consisted of milled wheat flour and maize meal, polished rice, oats, peas, navy beans, beefsteak, NaCl, and $CaCO_3$. The first generation did very well for about eight months, then failed rapidly. The 2nd generation failed very early without reproducing. Formula on page 351.

‡ Similar to 2153, but contained 10 per cent of cabbage. Family at first did well, but deteriorated rapidly with each succeeding generation. The 4th generation were in poor condition and had no young.

§ Similar to 2436, but contained no butter fat, and was alkalinized with $HNaCO_3$. Fertility good and infant mortality low, but each succeeding generation was decidedly smaller than its parents. The fourth generation was discarded in a stunted condition at the age of 2½ months. These experiments show the value of continuing observations over several generations, for they illustrate the tendency toward degeneration when the diet is faulty in even a slight degree.

TABLE XVI

Composition of Diets Used in Experiments Described in Table XV

No. of Experiment.	Beef-steak Grams.	Wheat Grams.	Maize Grams.	Oats Grams.	Peas Grams.	Navy Beans Grams.	Wheat* Flour Grams.	Corn† Meal Grams.	Rice‡ Grams.	Cabbage§ Grams.	Butter Fat Grams.	$CaCO_3$ Grams.	$NaHCO_3$ Grams.	NaCl Grams.
2436....	10.0	30.0	19.5	8.5	8.5	8.5			9.5		3.0	1.5		1.0
2153....	10.0			9.5	9.5	9.5	30.0	19.5	9.5			1.5		1.0
2069....	10.0			8.0	8.0	8.0	30.0	15.5	8.0	10.0		1.5		1.0
2360....	10.0	30.0	19.5	9.5	9.5	9.5			9.5			1.5	1.0	

* Bolted wheat flour.
† Degerminated corn meal.
‡ Polished rice.
§ Desiccated cabbage, subsequently steamed and dried.

to grow when nursed by these mothers, which were confined to faulty diets, was not the result of diminished milk production rather than of deviation of the secretion from the normal composition. It has not been found possible to secure complete information as to the actual amount of milk which any of these mothers secreted. The records of studies on women and on domestic animals, described in the early part of this chapter, afford abundant evidence that it is the quality which first falls off. Only when the lactating mother is brought to the verge of breakdown, does the flow of milk drop to a low level. The occurrence of infantile beri-beri rather than death from starvation, further serves to prove that it is milk of poor quality rather than of insufficient quantity which is responsible for the high infant mortality in those parts of the world where the poorer classes live too largely on food-stuffs derived from muscle meats and from plant products, the biological functions of which are those of storage organs. (See Chart X.)

374. **Breast Milk Not a Satisfactory Food Unless the Diet of the Mother Is Good.**—The statement, reiterated so frequently, that breast-feeding of infants is superior to the best system of artificial feeding needs, however, some modification. There are many women in various parts of the world whose diets are sufficiently faulty to interfere with the secretion of milk of good quality, and they accordingly supply their babies a food which must necessarily lead to retardation of development. An extreme case was observed by Andrews in certain women in the Philippine Islands, whose infants developed paralysis and died of beri-beri. The pathological condition was due to the fact that the mothers, while nursing, restricted themselves to a diet of a deficient type.

The carnivorous mother can produce milk of good quality when her diet contains sufficient amounts of glandular organs and bone in addition to muscle, blood and fat, but not otherwise. The omnivorous mother, to which class the human mother belongs, but too frequently attempts to nurse her infant while she subsists on a diet of muscle meats, bread made from degerminated and decorticated cereal, and potatoes and a few other articles which have analogous dietary insufficiencies. The occasional occurrence of scurvy in breast-fed infants represents an extreme example of specific starvation of the mother for a single dietary factor, and the resulting deterioration of her nursing infant. Physicians and nurses have repeatedly reported to me

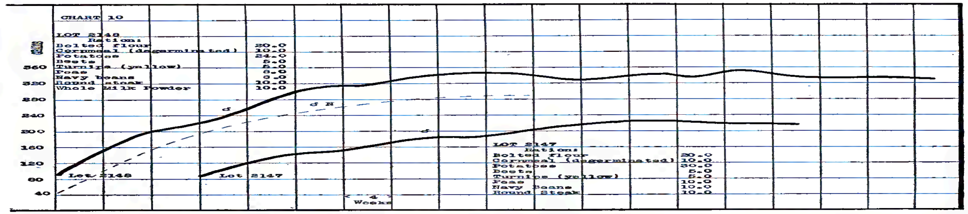

CHART 10.—The two curves in this chart serve to illustrate the remarkable superiority of whole milk as a supplement to a mixture of cereal grains, legume seeds, tubers, and fleshy roots as compared with round steak, a muscle meat. Lot 2147 had a complex vegetable diet of the type described, supplemented with a liberal amount (10%) of beefsteak. Their growth was slow and the animals never reached the full adult size. They also developed early in life the appearance of old age. Lot 2148 had essentially the same diet but supplemented with ten per cent of whole milk powder. This served as a source of mineral salts and of fat-soluble A, in which diet 2147 was deficient, and made possible much more rapid growth, larger final size and much longer life. These curves illustrate the importance of the proper selection of food, so as to be highly satisfactory, rather than the adherence to a diet which is somewhat faulty in one or more respects.

their observations that many women while nursing infants take for days or weeks, diets derived in great measure from tea, toast, sugar and other articles of food equally unfit for the elaboration of milk. The nursing mother should always have a diet of a quality calculated to insure a satisfactory composition of the milk which she is to secrete. This she can best realize by including in her menus liberal amounts of milk and of salads. It is not enough for the diet to yield a proper calorific value, furnish protein according to the long accepted standards, and afford variety and palatability. The specific dietary properties of the food mixtures which enter into the diet are of paramount importance and must be given due and weighty consideration.

375. **Rickets May Occur in Breast-Fed Infants when the Mothers' Diet Is Faulty in Certain Ways.**—Attention should again be turned to the observations of Hess (16) that the negro women of the Columbus Hill District in New York City, whose diets are derived almost exclusively from milled cereal products, tubers and muscle meats, fail to nourish their infants satisfactorily, as is shown by the almost universal prevalence of rickets among them. Because of the limited capacity of the digestive tract, it is difficult for the human being to correct the deficiencies of these products by the consumption of leafy vegetables as the sole protective foods. Milk is the most satisfactory adjuvant to the diet of the nursing mother for the correction of whatever deficiencies it is likely to exhibit in inorganic elements, quality of protein, and fat-soluble A. The inclusion of moderate amounts of raw fruits and of raw salad leaves and vegetables, is the best procedure for making available a satisfactory amount of the anti-scorbutic substance in mother's milk.

376. **All Who Escape Recognizable Nutritional Disease Are Not Well Nourished.**—It is of great importance to appreciate the fact that there may occur by reason of faulty diet serious damage to the young without the development of symptoms which definitely mark the patient as a sufferer from a deficiency disease. The latter cases are the rare exception. The most serious situation is that of hosts of children who suffer physical inferiority, and perhaps mental inferiority, abnormality of form and lowered vitality as the result of failure to secure in infancy and childhood a diet adequate to their needs. These children represent border-line conditions which usually pass unnoticed as cases of malnutrition. These are the children who frequently find their way into the school clinics and are forced

to repeat their work in one or more of the grades, and whose teeth serve as a source of lifelong annoyance. I do not desire to minimize the importance of the after-effects of infectious diseases as a factor in swelling the number in this type of children. In a very large number of cases, however, there can be no longer any reasonable doubt that the most fundamental problem is that of securing for these children a wisely planned diet calculated to raise their vitality to a higher plane.

377. **The Problem of Preventive Dentistry Largely One of Feeding During Infancy and Childhood.**—In an earlier chapter it has been shown how easily deviations from the optimal composition of the diet with respect to certain factors, leads to the development in the bones of histological changes easily demonstrable. These changes are prominent in rickets and kindred conditions. It should be fully appreciated by all, that the process of enamel development in the teeth, their eruption and nutrition is a part of the development of the osseous system, and is affected by the same factors that influence bone growth. If a tooth is poorly made, the best that can be done for its preservation is frequent repair. Teeth are developed and enameled before they are erupted, and these events take place during the last months before birth and following birth. During infancy the permanent teeth develop just under the milk teeth. The importance of providing at this epoch in the life of the child, an uninterrupted state of nutrition which is as nearly the optimal as possible, will serve as the most effective measure in providing in the child a dental equipment which will last well into old age and protect against the danger of invasion by microörganisms which now so frequently cause serious infections. Although it may sound prophetic at this time, when we have become so thoroughly schooled in referring almost exclusively the health problems of the human race to the field of bacteriology and parasitology, I cannot close this discussion without asserting that there is an even more fundamental, indispensable feature of health promotion than these. The basis for everything that is worth while in life lies in physical vigor, and as a means of securing for the young, the adult of the future, this priceless treasure, the importance of a properly adjusted dietary can scarcely be over-emphasized (17).

This chapter on the nursing mother strikes the keynote of this book, for it affords proof of the existence of and points the way to the remedy for one of the greatest sources of human ineffi-

ciency and suffering. Moreover, touching as it does the root of the evil effects of one of the most colossal errors of civilization, this chapter serves to illustrate most vividly the far-reaching importance of scientific nutrition in preventive medicine.

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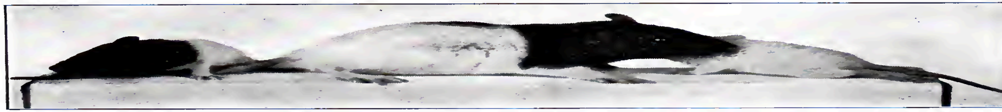

FIG. 18.—This illustration shows the great differences in the size, stage of development and vigor in young rats, which may result from faults in the character of the diets of the mothers which they are nursing. These three rats were the same age. The mother of the two little ones received a diet which was deficient in the quantity and quality of its proteins.

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CHAPTER XVI

NEW VIEWPOINTS RELATING TO PRACTICAL PROBLEMS OF NUTRITION

378. The Importance of Animal Experimentation to Human Welfare.—The sciences of medicine and surgery are built upon experience gained through animal experimentation. Almost all our knowledge of the rôle which bacteria play in the production of disease has been gained through studies on the lower animals. Protective serums could never have been discovered except by such procedure. Even now it is possible to diagnose some of the diseases most harmful to man only by the employment of rabbits or guinea pigs as test subjects, or for the production of blood having special properties for use in making laboratory tests.

The latest branch of medicine to develop is inspired by the prospect of preventing disease instead of the old ideal of curing the sick. This new field of preventive medicine owes much to animal experimentation. Natural vitality enables the tissues to resist the entrance of certain bacteria, and constitutes a most effective defence for the body against many agencies to which in an enfeebled condition it would succumb. Our knowledge of the profound effect which the diet may exert on the vigor of the body is almost entirely the product of observations of the effects of specially planned experiments on small animals.

The study of the science of nutrition as a branch of preventive medicine has not been sufficiently appreciated in the past. It is true that the carbohydrate content of the diet of the diabetic has for many years been regulated as a therapeutic measure. Food has been selected with a view to the relief of constipation. Liquid or soft diets have been provided for the sick in certain conditions. Anti-scorbutic foods have been provided for persons who were subjected to conditions which experience had shown were likely to induce scurvy. The avoidance of excessive food consumption has been recommended. A low protein diet, a purin-free diet, sour milk as a therapeutic agent, and other dietetic regulations have been resorted to as means of affording nourishment specially suited to peculiar conditions.

379. **Nutrition Has Assumed Greater Importance Than Ever Before.**—In recent years, however, new and surprising relations between food and health have become apparent. The relation between polished rice and beri-beri has been brought to light. Observations on the sequence of events as famine conditions are approached, have established the fact that as the last reserves of food are drawn upon epidemics of dropsy, cholera, pellagra, etc., develop and carry off the semi-starved population before they have time to die of starvation. The greatly increased sickness and mortality rates among civilians in warring countries has often been attributed to under-nutrition or to faulty diet, but the causes which brought about these conditions were understood only in a vague way. The debilitating influence of lack of sufficient food is easy for anyone to appreciate, but an understanding of the gravity of restriction to diets which are faulty in their chemical composition only in minor degrees is less easily acquired. Many well informed people who are accustomed to the critical examination of data have not infrequently shown a lamentably superficial conception of the relation of the character of the diet to health conditions.

380. **Many Are Still Unable to Grasp the Fundamentals of Scientific Nutrition.**—To-day few would dare to reject the array of experimentally established facts and deny the relation of beri-beri or scurvy to lack of some essential substances in the diet, or question that there is a high degree of specificity in the effects of the missing constituents which induce the development of these syndromes. Many, however, who consider themselves capable of passing sound critical judgment on health matters have attributed some of the nutritive disturbances seen in certain parts of Europe during the great war, to lack of sufficient fat in the diet when the latter was derived in great measure from cereals and potatoes, and have felt satisfied with thus disposing of the matter. In so doing they have ignored several other defects in such a restricted food supply which have within recent years become clearly demonstrated, but are still not generally understood. The experimental data discussed in earlier chapters leaves but small room for doubt that lack of fats, strictly speaking, had little or nothing to do with health conditions. It was a lack of the substance fat-soluble A, which certain fats of animal origin contain in abundance, but which vegetable fats and oils derived from oil-bearing seeds either lack entirely or at best supply but very inadequate amounts, which

was responsible for such nutritive disturbances as could be attributed to lack of fats in the diet. This view is supported by the observation of Wells (1), who observed remarkable benefit through the administration of small amounts of cod liver oil to malnourished Roumanians whose eyes were damaged by faulty diet. In many places, it would doubtless have been possible under wise management, to have corrected the defect due to lack of fat-soluble A in the diet by a liberal use of leafy vegetables, although these contain no more fats than do the cereals.

There were operating at the same time to produce malnutrition, other factors essentially as important as the lack of fat-soluble A in the diets just described. These were a low intake of protein of relatively low biological value, and lack of sufficient amounts of certain mineral elements, especially calcium and phosphorus and a low anti-scorbutic value of the foods employed. These deficiencies were doubtless on a parity with lack of fat-soluble A in causing lowered vitality, ill-defined cravings of the appetite, gastro-intestinal disturbances, and interruption of growth and faulty skeletal development in children.

381. There Is Need of Popularizing the New Knowledge of Nutrition.—The lack of understanding of the way to solve the practical problems of alimentation which were forced upon Europe by the war is easily appreciated when we consider how new the science of nutrition is. The literature relating to the phases of the subject which were understood was confined to scientific journals. Few of the men who became officials in the armies had any knowledge of nutrition other than that relating to calorific and protein requirements. Under the trying conditions of war there was little time or opportunity to acquire or apply new knowledge, and no great incentive to seek anything beyond bare subsistence except in those members of the population who contributed directly in some manner to military success.

It is not easy to overlook the short-sightedness and to forgive the damaging propaganda of certain specialists concerned with public health work who hold that there is no reason to believe that there is any important relation between the character of the diet and the health of the individual except under circumstances where the faults of the diet are extreme. Some have insisted that the great increase of tuberculosis in Europe since 1914 is no evidence that under conditions more nearly approaching normal, the character of the diet is a factor of importance in predisposing one to this disease. The view is held that at a

certain point of severity in malnutrition the vitality breaks down, and the body becomes a prey to diseases due to the invasion of micro-organisms, but that up to this critical point the diet plays little, if any, rôle in the etiology of infectious diseases. There is much reason to believe that this conception is not generally applicable and that it applies only to a certain group of infections. There are many grades of malnutrition between the optimum well-being on the one hand and on the other, such extreme conditions as are recognizable by the clinician.

382. **Entire Subject Must Be Viewed from a New Angle.**—In order to appreciate the viewpoint which is established by recent researches on foods and nutrition it is essential to fully understand the great advantages which we now enjoy in being able to think of foods in an entirely different way from what was possible a few years ago. Ten years ago the crude comparison of alimentation with the stoking of an engine seemed satisfactory to most teachers. This is no longer a suitable figure for conveying to the student of nutrition the conception which it is desired he should gain. Little more than a decade ago it was supposed that a chemical analysis of a food for protein, carbohydrate, fat and mineral salts, was sufficient to reveal its biological properties. Certain standards of composition had become established on the authority of experts, and it was believed that if any food fulfilled the requirements of these standards with respect to total digestible nutrients, available energy and protein content, it could be counted upon to meet the nutritive requirements of the body. In Chapter II it has been described how after the year 1900 many attempts to nourish young animals on food mixtures made up of purified substances, and including the approved amounts of all the components of foods which the chemist was called upon to estimate, proved utter failures, and demonstrated the inadequacy of a time-honored theory.

383. **Types of Experimental Observations which Made Nutrition a New Science.**—The early experimental work with diets consisting of relatively pure food substances had for their objective in many instances, the demonstration of the inadequacy of such "incomplete" proteins as gelatin or zein, or the relative merits of phosphorized and non-phosphorized proteins. There was a period when a series of papers were published by physiological chemists debating, on the basis of rather poorly planned experimental work and its results, the question as to whether phosphorus in the form of organic compounds such as lecithins,

or phosphorized fats, the nucleic acids found in the nuclei of cells, and in phosphorized proteins such as casein of milk or vitellin of egg yolk, was superior in its nutritive value to the phosphorus of mineral salts such as calcium phosphate. The view was supported that for the construction of the highly organized structures of the body tissues such as nuclear substance, complex phosphorus-containing fats, etc., it was essential that similar highly organized phosphorus compounds should be available in the food. It was generally conceded that bone could be formed from inorganic phosphates, but most investigators doubted whether this form was as valuable as organic phosphorus in animal nutrition. This subject was for years a prominent one for discussion, although there never was a single well established fact to support the view that the highly organized forms of this element which occur in plant and animal tissues are superior in animal nutrition to the simple mineral salts of phosphorus. In 1909, as has already been described (2), McCollum first published experimental work which finally disposed of this entire question, by showing that young rats could grow on diets containing phosphorus only in the form of calcium phosphate derived by grinding the naturally occurring mineral.

384. **The Experiments of Hopkins.**—The experiments of one investigator, Hopkins (3), were of a different type from those mentioned in the preceding paragraph. He met with complete failure in his attempts to nourish young animals on purified protein, carbohydrates, fats and mineral salts, but was able to induce growth with the same diet supplemented with small additions of milk. The milk furnished some substance or substances which were not present in the mixture of purified food substances, and which were essential for growth or the maintenance of health. It has been pointed out how Hopkins recognized the significance of his discovery and designated the unknown substance or substances which the milk furnished to the advantage of his animals, as "accessory" food substances. These experiments were conducted in 1906 but were not described until 1912. In the meantime Holst had made his classic demonstration of the relation of scurvy to diet, and Funk and Suzuki had come forward with their extension of the studies of Eijkman and of Schaumann, and had coined the terms "vitamine" and "oryzanin" respectively. In the minds of many nutrition investigators these were observations in the field of pathology rather than of normal nutrition.

The results of the feeding experiments with cattle described in Chapter II are sufficient to illustrate the fact that studies with ordinary foods such as wheat, maize, etc., could never have been made to reveal the secrets which lay hidden in the field of nutrition. The results of those studies amply demonstrated that the persistent efforts of McCollum and Davis from 1907 to 1915 in seeking to discover the reason for the failure of young animals to grow on diets consisting of purified food substances was the most profitable line of attack for securing an insight into the number and natures of the factors which enter into the make-up of an adequate diet.

385. **Difficulties of Solution of the Fundamental Problems of Nutrition.**—Simple as the discussion of the adequate diet appears to be in the present state of our knowledge, it was a most difficult task to bring order and understanding into the field of nutrition. In experiments with the rat using simplified and purified food substances such as were necessary for solving the problems of what constitutes the simplest adequate diet, the difficulty in succeeding was much greater than one would at first thought suppose. The small prospect of success will be better appreciated when it is realized that there were, for the nutrition of the rat, two indispensable dietary factors whose existence were hardly more than suspected by students before that time. These were the anti-ophthalmic and anti-neuritic substances, fat-soluble A and water-soluble B, respectively. In addition there were three variable factors whose importance was appreciated in a general way, but for which no satisfactory standards had been established. These related especially to the quality of the protein, the concentration of the several mineral elements essential to normal nutrition, especially calcium and phosphorus, but also in an important degree to the content of sodium and chlorin in the diets. Any one or more of these factors might easily be so constituted as to determine the failure or success of an experiment. If the purified protein happened to be of relatively poor quality, the amount of it included in the diet might easily be too scanty to support growth, yet it would be impossible except through the conduct of a considerable number of experiments, to gain a satisfactory insight into this matter. If, in deciding on the amount of calcium to introduce into an experimental diet, it was assumed that a cereal, such as wheat, probably contained a proper amount to meet the nutritive needs of an animal, this error would have foredoomed the resulting growth experiment to failure, even if an abundance of protein of good quality,

and vitamins in liberal amounts were supplied, and satisfactory adjustment of every other constituent of the food was by good fortune realized. A similar statement may also be made regarding phosphorus, but the shortage of this element is not so serious in most vegetable or animal foods, and if the investigator was guided by the content of phosphorus in ordinary cereals in arriving at a decision as to how much of this element to include, a less serious error was likely to be made. Even the failure to add a sufficient amount of common salt would have been disastrous to such experiments as we are discussing, the object of which was to find just what elements and complexes are indispensable in a diet, and to prepare the simplest possible food mixture which could support growth and normal well-being. Such studies required much time and labor in the preparation of carefully purified substances, and failure in a considerable number of attempts would be expected to lead to discouragement and cessation of effort to solve such a problem since the chances of success would seem so remote.

When it is appreciated that there was no other possible method of attacking the solution of this problem than the conduct of a series of feeding experiments with simplified diets, and the interpretation of the results on the basis of whether the animals in numerous groups grew or failed to grow, it will be conceded that the prospects of succeeding in arriving at an understanding of the essentials and non-essentials of an adequate diet were very remote. By good fortune, however, this problem was successfully solved in its broad outlines, and further detailed researches can now be undertaken with definite aims and the guidance of an adequate theory.

386. The Method of Interpretation of McCollum and Davis.—In 1915 McCollum and Davis published two papers which described a satisfactory method for interpreting such experiments. They gave two convincing demonstrations of the applicability of their theory of interpretation, which has formed the basis of all the more important nutrition studies since that time. One of these was a description of a successful growth experiment with young rats fed a diet consisting of purified protein, carbohydrate and mineral salts supplemented with such a fat as butter fat, together with an extract of a natural food which contained the anti-neuritic substance. The same diet without the extract proved a failure, as it also did when a vegetable fat or the body fat (lard) of animals replaced the

butter fat. An adequate amount of fat was not the necessary element, but rather the right kind of fat, or fat which contained in solution some substance which is essential for the normal functioning of the body. This experiment demonstrated also that a second substance, the anti-neuritic factor, was equally indispensable with the one furnished by butter fat. The second demonstration of the validity of the view which was expressed as to the essential components of a diet was made with polished rice. It was clearly shown that in order to make this degerminated and decorticated food grain complete from the dietetic standpoint it was essential to supplement it with a protein to make good the shortage of this factor; with certain mineral salts, and with a growth-promoting fat and an extract which furnished the anti-neuritic substance.

387. **It Was a Piece of Good Fortune That the Earliest Experimental Studies Were Made with the Rat.**—It is further of interest to point out, in the light of our present knowledge that if the rat had been susceptible to the disease scurvy, these experiments would both have ended in failure and no possible explanation would have been apparent, for in both cases the series of diets employed were lacking in the anti-scorbutic substance which is essential for the normal nutrition of certain species such as man, monkey and guinea pig. Fortunately for progress in this branch of science, the rat is immune to scurvy, because he can synthesize the anti-scorbutic substance from other complexes in the food. For the demonstration of the nature of scurvy and its relation to faulty diet, it was necessary to employ another species of animal, the guinea pig, as an experimental subject.

388. **An Adequate Diet May Be Remarkably Simple.**—From what has been said it will be appreciated that a diet may be remarkably simple, viz.: consist of a single purified protein, a source of the sugar glucose, nine mineral elements and two uncharacterized dietary factors, and be entirely adequate for the support of growth and prolonged well-being in the rat. From relatively simple substances the animal tissues are capable of synthesizing many compounds of extraordinary complexity. The limitations of the tissues are, however, sharply defined, and if the circulating fluids which constitute the environment of the living cells, deviates appreciably from very definite composition, the efficiency of their functioning is lowered, and their vitality affected. The degree to which they are affected can serve as

a measure of the extent of the departure of the diet from the optimum, provided the right kind of observations are made to bring this to light.

389. **Great Stimulus to New Investigation During the Last Few Years.**—The line of study which was pursued by the author led to the formulation of the above described working hypothesis which has so effectively served as a guide to the interpretation of experimental data since that time. This clear-cut statement of the essential factors which the diet must furnish in order to maintain normal nutrition served to enable anyone to study the dietary properties of any food substance or mixture, using animals as test organisms, rather than through the use of chemical methods. The result of this change in the method of attack on nutrition problems was that there has been more advance in this field since 1915 than in many years before. It made possible the development of the biological method for the analysis of a food-stuff. This method gives exact information as to the quality of every factor which contributes to the success of the nutrition of an animal. This method has been described in Chapter II, p. 27. *As the result of the accumulation of data of this type we have come to look upon foods in a new way. Instead of classifying them on the basis of their protein, or fat, or carbohydrate content, as was formerly done, we classify them on the basis of their biological properties as foods.* Those which are faulty in similar respects are classed together, irrespective of their chemical composition. Thus the bean with twenty-three per cent of protein, is logically classed with the potato which has but two per cent, because the bean proteins are of very poor quality and are of little use for the promotion of growth or for the repair of tissue waste. The classification referred to, however, was the outcome of the discovery that all vegetable foods which have the function of storage organs (seeds, tubers, fleshy roots) have similar dietary properties and similar deficiencies regardless of their chemical composition as revealed by the standard food analysis. The highly specialized muscle tissue falls in the same class with the cereals in respect to its dietary properties, and differs very markedly from the glandular organs just as do the seeds, tubers and fleshy roots from the vegetative parts of the plants, the leaves.

390. **Vegetable Foods Having Similar Biological Functions Have Likewise Similar Dietary Properties.**—Since mixtures of foods having similar deficiencies cannot greatly enhance each

other's values in meeting the nutritive needs of an animal, we should expect, from the properties of the foods of the seed, tuber, fruit, root and muscle tissue group, that combinations of any articles belonging to this class, should not form a satisfactory food supply. Experience has now amply demonstrated that this is the case. The conclusion is warranted, therefore, that it is wise to select foods from different groups, based upon their nutritive qualities in order to properly balance the resulting mixture so as to make it near in its constitution, what the animal body needs for its proper maintenance. Numerous feeding experiments have shown the wisdom of this plan. Most food substances now in common use do not supplement each other in a very effective manner. Milk, and the thin leaves of plants are of especial value for enhancing the dietary properties of nearly all other foods, and they are therefore of particular interest and importance. It was for this reason that I have termed them "protective foods." In a lesser degree, eggs and the glandular organs of animals serve this purpose of improving the quality of cereals, tubers, fruits, roots and of meats of the muscle type, but this improvement is incomplete, because of their lack of sufficient calcium.

The above statement regarding the inadequacy of a diet derived from seeds, tubers, fleshy roots, fruits and muscle meats, is made again as in the first edition of this book, notwithstanding the assertions of Steenbock that certain yellow pigmented root vegetables, such as carrots and yellow turnips, and yellow maize, as contrasted with white or red varieties, are decidedly richer in fat-soluble A. There appears good reason to believe that certain varieties of vegetables are superior to certain others with respect to their content of fat-soluble A, and apparently yellow maize represents a case where the yellow pigment accompanies the superior nutritive property. The idea that the anti-ophthalmic substance is related to, or associated generally with the yellow pigments of plants has been conclusively disproved by the work of Palmer and his associates (4). But even if the statement is accepted that certain varieties of vegetables can serve as an adequate source of fat-soluble A, it would not alter in any way the truth of the generalization that diets containing yellow pigmented products would not prove satisfactory. The diets of this character would be deficient in certain mineral elements, and sufficiently so to make it impossible to secure normal development in young animals. The first of these in importance

would be calcium, but sodium chlorid and phosphorus would also contribute, by their relative deficiencies, to prevent the normal nutrition of the animals.

391. **Early Nutrition Investigators Ignored Human Experience with Diets of Different Types.**—It is remarkable that physiologists and others who were interested in the subject of nutrition, failed for so many years to appreciate evidence so abundant in human experience, that the proper selection of food was a most important means of improving or preserving health. Beri-beri incapacitated many millions of people during the centuries before its cause became known. It certainly occurred in Japan two centuries before the Christian era. It was not, however, until Eijkman, in 1897, compared the effects of different kinds of rice used as human food in Java, on pigeons and poultry, that a clue was gained as to the actual cause of the disease.

It had been appreciated for more than a century by some people that certain fresh fruits and vegetables would effect a cure of scurvy, and that it attacked only those who were restricted for a time to a diet of stale or cooked foods. It was not until after 1900, however, that Holst brought out clearly through his experiments, on animals, the fact that cooked and dried foods were scorbutic and that fresh vegetables had a most extraordinary power to induce relief of the symptoms of scurvy. The nature of the cause of scurvy could not be discovered by experiments with the rat, since it is not susceptible to this disease. The guinea pig is especially well adapted for this purpose.

Eye lesions varying from mild to distressing nature have been common in several parts of the world for many years. No student of nutrition suspected that there was any cause for these other than infection until the relation of one type to specific starvation for fat-soluble A was established. McCollum and Simmonds showed clearly that the keratomalacia or xerophthalmia which had been observed by several investigators who had restricted rats to faulty diets, was due not primarily to infection, but was of specific dietary origin and results from lack of fat-soluble A. It is, therefore, a symptom of a deficiency syndrome comparable to beri-beri or scurvy. Human diets are always too complex to admit of interpretation as to their deficiencies except on the basis of carefully planned experiments on animals. It was for this reason that it was impossible for the earlier investigators to discover the true causes of the so-called deficiency diseases. Experimental studies with diets composed

of purified food substances formed the key to the complete understanding of the natures of the etiological factors in each of these syndromes. Perfecting the biological method for the analysis of a food-stuff, formed the foundation of our knowledge of how to combine our natural foods so as to prepare diets which fall little short of the ideal in their capacity to induce optimal nutrition.

The rapid development in the course of a decade, of a satisfactory understanding of the fundamental principles of nutrition, and the manner in which satisfactory diets can be planned, constitutes one of the greatest triumphs in the whole field of science. To-day the whole subject seems relatively simple, and the student of to-day is likely to forget that but a decade ago, protein content, fuel value and digestibility were the only factors deemed of much importance in the discussion of food.

392. **Scientific Nutrition of Greater Value in Preventive Medicine Than in Cure of Disease.**—The researches in the field of nutrition have a greater value in preventive medicine in relation to raising the vitality of mankind, with all that this implies, than they have in the prevention of the occurrence of the deficiency diseases. This fact has never been sufficiently appreciated. In the aggregate, by far the most important effect of faulty nutrition in man is the result of errors of one kind or another which are not sufficiently grave to cause prompt and spectacular failure. It is the gradual operation of more or less constant, but unperceived causes, rather than of great and marked exposures of an accidental nature which in nearly all cases are responsible for undermining the health of the individual. Of these causes, it now seems certain, the consumption of an improperly constituted diet is one of the most important. It is the cause of inferiority in physical development, instability of the nervous system; lack of recuperative power and endurance and consequent cumulative fatigue, and lack of resistance to infections such as tuberculosis and other types where specific immunity is not easily developed by the body. In addition to these the rate of development of senile characters and consequently the length of the span of life, are greatly influenced by the type of diet employed. It is important for us to inquire how far such defective diets as result from unwise selection of ordinary foods, can influence the life history of man and animals.

393. **An Effort to Duplicate Human Experience with Diet with a Rat Colony.**—Some years ago the idea occurred to me

that we had progressed sufficiently far in our investigations to make it possible to duplicate human experience as relates to diet, with our colony of domestic rats. A systematic attempt has been made to do this. All factors other than diet, such as temperature, ventilation, illumination, cleanliness and opportunity for exercise, were uniform in these experiments. The only factor in the lives of the animals comprising the different groups which was different, was the character of the diet. Such variations as were observed in the physical development, fertility, capacity to produce milk of satisfactory quality and in sufficient amount for the nutrition of the young, length of life and age at which the first signs of senility appeared, can safely be attributed to the character of the diets employed. We had available to aid us in the planning of the diets the extensive data obtained in the application of the biological method for the analysis of a food-stuff. All the more important natural foods employed in human nutrition in the north temperate zone had been examined by this method. In each case we were able to state definitely the nature of the fault or faults in the diet, and the extent to which each departed from approximately the optimum in quality. These experiments afforded data which are of more than ordinary interest when we consider the parallel in physical development, and in such other points of comparison as can be drawn between man and the lower animals.

394. **Important to Secure Effects of Diet on Life History.**—We came to appreciate some years ago, that we were able to demonstrate in short experiments only faults of a pronounced nature. This is what is to be expected. If the tissues are subjected to only slight deviations from the optimum in their food supply, they will not deteriorate rapidly as they do when the faults in the diet are more pronounced. It was to be expected, however, that longer periods of observation would reveal defects of a lower order. This we have found to be the case. There was a time a few years ago when any investigator of a nutrition problem would have said that a diet which was adequate for the support of growth through a considerable portion of the period during which growth normally takes place, would certainly be adequate for the maintenance of health and vigor in the adult. The experiments with domestic animals conducted at the Wisconsin Experiment Station, clearly forecasted the necessity of including reproduction records as a means of refining the technic of nutrition studies so as to make possible more accurate esti-

mations of quality in one or more factors in the diet. Miss Simmonds and I have developed this idea and have applied this principle in our work since 1915. We realized the importance of attempting to answer the question: How sensitive is an animal to faulty diets of different types? Will not faults in the diet which are too slight to affect the animal promptly during the growing period to an extent which will be observable, become easily apparent if they exert their influence upon it at a time when it is meeting the unusual demand occasioned by pregnancy or the nursing of young? Will not the growth and well-being of the young and the capacity of a family to remain in a state of vigor during succeeding generations when confined to a certain type of diet, reveal shades of quality not to be discriminated in a short experiment? We have now tested these propositions sufficiently to enable us to give very definite answers to them. The results have amply demonstrated that any fault in the diet, however slight, which causes it to deviate from the optimum, will, if it exerts its influence over a sufficient period, surely be reflected somewhere in the life history of the individual or its descendants. The sensitiveness of the rat to faulty diets, which fall but little short of the optimum, is remarkably great, if such diets are persisted in for considerable periods. In certain critical conditions such as pregnancy, such effects become observable in a short time. The nursing period is almost equally critical in that small departures from the optimum composition of the diet leave their mark on the vitality of the young and frequently also on the vitality of the mother.

395. **Impossible to State the Minimum Requirement of Any One Food Factor Unless All Dietary Factors Are Evaluated.**—We have reached the conclusion that it is not possible to state the amount of any food factor which constitutes the minimum or the optimum, or an excess, without taking into consideration the biological values of each of the other factors in the diet. The minimum amount of any dietary factor of constant quality, which will just serve to maintain apparently normal well-being, will fail to suffice when another factor is modified so as to be less satisfactory, and after such a modification of the diet, increasing either of the two factors under consideration will suffice to protect the body from harm in some measure. *There is a principle of relativity which is of fundamental importance in estimating the value of a diet as a whole.* The diet must be considered as made up of a number of factors, and an effort

made to adjust each factor at the optimum. Long observation of the type of experiments here described, serves to reveal when animals are brought into a "twilight zone" of nutritional instability, but in which there is no external evidence that they are not in the optimum condition.

396. **Remarkably Accurate Estimations of Nutritive Value Are Possible by Animal Experiments.**—The results of observing animals beyond the completion of growth, to determine their fertility, success in rearing young and the rate at which they developed the characteristics of old age, were so striking that we extended our observations to include restricting single families to a monotonous diet through several generations. This brought to light the fact that a diet may be sufficiently good to enable an animal to grow in a perfectly normal manner, and to exhibit a moderate amount of fertility, yet with each succeeding generation the progeny becomes smaller and less well developed physically, and after two, three or four generations the strain dies out. Several comparable examples of similar experience in man may be cited. Campbell (5) stated that among the poorer classes in the slums of English cities, the family never passes beyond the third generation. Galton (6), in a statistical analysis of one thousand town families and one thousand country families selected from the town of Coventry and the surrounding rural population, found that the town population supplied to the succeeding generation but three quarters of the number supplied by a similar number of country people. In two generations the adult grandchildren of the town dwellers amounted to but little more than half the number of descendants of the country dwellers. The employed urban dwellers are continually being recruited from country stock, and themselves tend to die out. Food is cheaper in rural districts and the selection and quality is distinctly better generally speaking, than it is where the supply is derived almost entirely from the grocery store. The grocer carries a surprising proportion of stock derived from cereal grains, legume seeds, fruits, tubers and muscle meats. It has already been emphasized that food-stuffs from this list cannot be combined so as to constitute a satisfactory diet. The behavior of our rat population when restricted to diets corresponding in their origin to those of the urban dweller of either England or the United States, will be described immediately below. The extent to which the rat has proven to be sensitive to even small modifications of the nature of its diet is

truly amazing. It suggests that it is much more important than has been hitherto believed, to have the diet nicely adjusted with respect to all its essential constituents, in order that the development shall be as nearly the optimum as possible. It is under such conditions that the characteristics of youth are preserved as long as possible, and the span of life prolonged.

397. **A Specific Illustration of the Effects of Faulty Nutrition.**—As an illustration of the extent to which we can control the life history of a group of experimental animals, we may take the effects of a diet consisting of degerminated cereal products such as bolted wheat flour, degerminated corn meal and polished rice, whole wheat, maize meal, rolled oats, potatoes, peas and beans. Irrespective of the proportions in which the foods listed are combined, the resulting mixture will contain proteins of relatively poor quality. Its content of calcium, phosphorus, sodium and chlorin will be decidedly below the optimum. It would be very deficient in the organic factor, fat-soluble A. The larger the proportion of milled products introduced, the greater will be each of the deficiencies enumerated. In order to make our illustration as striking as possible, let us take a mixture consisting to the extent of about 50 per cent of degerminated wheat, maize and rice products, the remainder being derived from the entire cereal grains and legume seeds.

On such a food supply young rats would fail to grow. They would develop deformities which are characteristic, the body being too short and stocky, and the thorax more or less collapsed, and misshapen. Their lives would be measured by a very few months at greatest.

With the same basal mixture, supplemented with small amounts of butter fat to furnish fat-soluble A, and the mineral elements in which the food is deficient, in amounts so small as to only partially correct the deficiencies of the diet, we could easily, from experience, adjust these corrective additions so as to enable us to predict that the group of young rats fed this second diet, would grow at about half to two-thirds the normal rate to something like two-thirds the normal adult size, after which they would remain stunted. Within a few weeks after the cessation of growth, the animals would show distinct signs of poor nutritive condition. Their hair would be harsh and rough. The animals would lose the normal solicitude about grooming themselves, and would become unclean looking. They would never have any young, but would steadily deteriorate and

die at a very early age, about six or seven months. (See Chart 11.)

398. **Effects of Diet in Determining the Span of Life.**—The extreme span of life of the rat under highly satisfactory conditions of nutrition and hygienic surroundings is about thirty-six months. Probably two-thirds of all animals kept under the best laboratory conditions would die before reaching the age of two years. In the group of animals just described, therefore, the span of life was reduced to about one-fourth to one-sixth of its extreme limit, as the result of faulty nutrition caused by a diet in which no essential was entirely lacking, or lacking to a degree which would cause the development of a specific deficiency disease.

Employing other portions of the basal food mixture described, and in preparing these portions for feeding a series of experimental groups of young rats, we could, in the light of our experience, add such amounts of a growth-promoting fat, and of the several mineral elements in which the food is deficient, as to form a series of diets which would be progressively nearer and nearer to the optimum in the character of each of the essentials for optimum nutrition. When several groups of young rats were confined to these diets we could confidently predict that they would differentiate, one group from another, in their length of life. All would be able to grow to the full adult size, and while they were growing they would appear to be perfectly normal animals with bright eyes and glossy coats. The interval following the completion of growth and preceding rapid decline would be determined by the extent to which, in any single case the faults in the food mixture were corrected by suitable additions. Thus we could make them last six months, ten months or twenty months after they ceased to grow before they would appear old and rough looking and would show the irritability characteristic of most old rats.

399. **Fertility and Infant Mortality Are Valuable Indexes to the State of Nutritive Well-Being.**—In the case of those groups where the state of their nutrition was sufficiently good to enable them to show a moderate fertility, it would be observed that the infant mortality would be higher the more deficient the food mixture. On such diets partly corrected by suitable additions the infant death rate has been uniformly 100 per cent. Another group with additions more nearly approaching the optimum will rear 40 to 60 per cent of their young, while the same basal mixture, fed supplemented with the right amounts

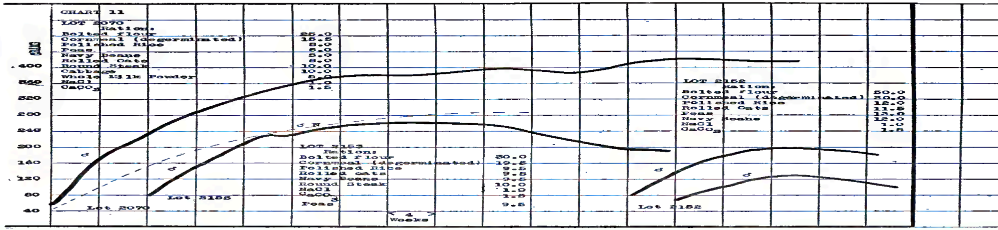

CHART 11.—The three curves shown illustrate the lack of fat-soluble A and the low quality of the proteins in a mixture of milled cereal products and legume seeds. In each experiment the chief mineral deficiencies were corrected by the addition of sodium chlorid and calcium carbonate. Lot 2152 had a diet which contained proteins of poor quality and was deficient in fat-soluble A. Note that the animals grew but little, and began very early to fail as shown by loss of weight. Their entire lives were not longer than the period during which a well fed rat normally grows.

Lot 2153 had a diet essentially like that of Lot 2152 except that its proteins were enhanced by the inclusion of round steak. The diet was still deficient in fat-soluble A although by no means lacking in it. Growth was rapid for a time but the full adult size was never reached, and the animals early developed the characteristics of old age.

Lot 2070 had essentially the same diet as Lot 2153 except that cabbage and whole milk powder (Merrill-Soule) were included. These served to further enhance the proteins and to furnish fat-soluble A in moderate amount. The result is very spectacular. The animals grew rapidly to large size and maintained for a long period the characteristics of youth.

of the substances in which it is deficient will produce a group of adult rats which will scarcely lose one litter in a hundred.

Formerly in our colony the terminal event in the lives of many of the animals restricted to such deficient diets as have just been described, was a lung infection caused by streptothrix. As the animals lost their vitality through restriction to faulty diets they became more and more a prey to the disease. With selection of vigorous breeding animals and with cleanliness we have succeeded in greatly reducing the occurrence of this infection.

When the diet is made sufficiently good to enable the rats to rear only a fair amount of their young, there is a strong tendency for the animals to be smaller with each succeeding generation, until within three, four or five generations they fail to reproduce and the strain dies out. All the experimental groups described, it should be remembered, would have been sufficiently well nourished to enable them to grow to two-thirds to full adult size, and to appear normally nourished while they were growing, yet dietary deficiencies of no greater magnitude than those we are here discussing, may profoundly influence the life history of the individual or the history of the family.

Using the degerminated cereal, and whole cereal, and legume seed mixture described as the basis of the experimental diets just discussed, it would be necessary to add about 1.5 per cent of calcium carbonate; 1.0 per cent of sodium chlorid; perhaps enough of some phosphate to furnish about half of one per cent of the phosphate radical, to make the diet complete with respect to its mineral content. The addition of 3 to 5 per cent of butter fat or 2.0 per cent cod liver oil, and 15 per cent of a purified protein, casein for example, would complete the organic portion of the ration and would constitute a highly satisfactory food mixture through many generations with no noticeable deterioration of the race on account of monotony of food supply. How strikingly similar is the history of such a series of animals on carefully graded diets, to the experience of the urban dwellers of England, which Galton describes. (See Chart 12.)

400. **One May Have a Surprising Variety of Food and Still Have a Faulty Diet.**—The most surprising generalization which is warranted by exact nutrition studies, is that even a diet composed of cereal grains, legume seeds, tubers, fleshy roots, fruits and muscle cuts of meat, irrespective of the proportions in which the components are represented, the variety which it affords, or the chemical composition as shown by even the most searching

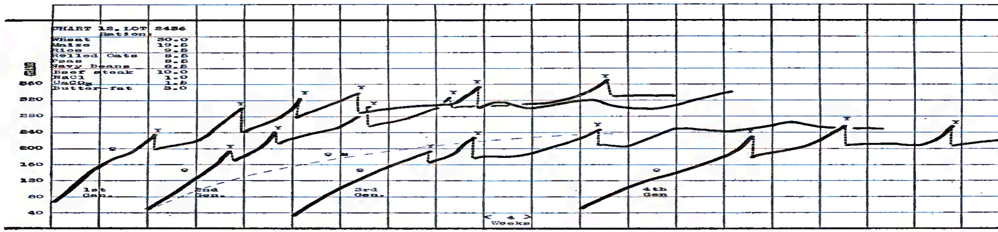

CHART 12.—This chart shows how good growth and high fertility may be secured in rats on a monotonous diet consisting of cereal grains, legume seeds and beefsteak supplemented with calcium, sodium and chlorine and with a source of fat-soluble A. If the inorganic additions are omitted the animals on this diet would be entirely unable to grow. If the butter fat were omitted they would be very inferior, and succeeding generations would be of low vitality. This would also tend markedly to reduce the fertility. If the beefsteak was omitted and no other supplementary source of protein was added in its place the animals would again be stunted, especially in the second generation. The omission of a supplementary source of protein would effect in a marked manner the capacity to produce and rear young. With the diet as tabulated, however, we have a complete food mixture and the family took it without any variation through successive generations without any striking deterioration in vitality.

analysis by chemical methods, will fail to support satisfactory growth in a young rat. It will further fail to maintain satisfactory health and vitality in an adult which has been reared on a diet which is of high quality until it has completed its growth, and is later transferred to its experimental diet. Such a diet may contain any or all of a list of foods including wheat, maize, rolled oats, barley, rye, pea, bean, soy bean, potato, turnip, radish, beet, steak, ham, roast, etc., or any other seed, tuber, root, and muscle meat, and still fail signally to maintain the vitality of a rat. Muscle meats, as has already been stated, enhance such a mixture only with respect to protein and phosphorus, among the factors in which it is deficient. When such meats are included in the above list, the deficiencies of the diet will be limited to calcium, sodium, chlorin and fat-soluble A. In the above discussion we have limited ourselves to the nutrition of the rat. This species, as has already been pointed out, does not require the anti-scorbutic substance in its diet. In order to make such a food supply as we are now discussing, complete for human nutrition, it would be necessary to include a certain part of the fruit in the raw condition. Raw potato and other root vegetables would also serve this purpose well, whereas the seeds of the cereals or legumes, or muscle meats, are of very little value for this purpose.

401. Any Diet Which Is Unsuited for the Promotion of Growth in the Young Will Not Be Satisfactory for the Maintenance of Health in the Adult.—The question naturally arises in the mind as to whether a diet may be satisfactory for the maintenance of optimal nutrition in the adult, but unsuited to the nutritive needs of the young. We have sought to gain an answer to this question. By restricting youthful adult animals to diets which were known to be incapable of supporting growth in the young, we have convinced ourselves that there is no important difference in the nutritive requirements of the young and the adult. Any diets which we have studied, which were not satisfactory for the promotion of growth in a young rat, were found to cause some damage to adults which were restricted to them. This might be manifested in early aging, short life, lowered fertility or the deterioration of a family restricted to it through several generations. We are of the opinion, therefore, that any diet which is not suited for the promotion of optimum nutrition during growth will fail to support an animal so as to induce a long span of life, and sustain the optimal well-being over a long period.

402. Effects of Faulty Nutrition on the Attitude of the Mother Toward Her Young.—The reaction of mother rats toward their young, when confined to certain types of faulty diets, especially those low in protein, is especially interesting. In many such cases the mothers react abnormally toward their young and destroy them soon after birth. The normally nourished rat practically never destroys her young, but is on the contrary, very solicitous for their welfare. We have taken mothers which have destroyed two or three litters, and changed their diet for the better, and have seen them thereafter produce other young and care for them in the normal manner. Miss Simmonds and I are inclined to regard this as especially significant. It involves breaking down one of the most fundamental attributes of the nervous system, viz.: the maternal instinct, and the development of infanticidal tendencies, through disturbance of the proper balance between certain factors in the diet.

403. A Poorly Nourished Population Tends to Be the Product of Individuals Young in Years.—Many animals on diets which are faulty in some degree, show reduced fertility or even remain sterile. When the fertility is greatly reduced it is usually the case that any young which are born are produced while the mothers are still young. When fertility is low the litters tend to be smaller than normal, and as a rule, although not invariably, the intervals between litters is abnormally long. Sterility may be independent of physical vigor, so far as the condition of the animals can be judged, and may exist in spite of sexual activity in the female. We have frequently observed in male rats which were rendered prematurely old as the result of deficient diet, atrophy of the testes. Osborne and Mendel (7) have made similar observations on rats fed liberally with yeast. Although not invariably true, one may say that in general, the adherence to a diet which is much below the optimum in quality with respect to one or more factors, restricts fertility to early life, and leads to the perpetuation of the species by individuals which are chronologically young, although they may be considerably advanced in respect to physiological deterioration.

404. The Poorly Nourished Individual Tends to Hurry Through His Span of Life.—We interpret the observations we have made on the influence of monotonous diets falling below the optimum in quality, and failing, therefore, to maintain satisfactory nutrition over a prolonged period, to mean that when the diet is faulty the individual, in effect, tends to hurry through its life history, and each phase of its history is shortened. The

tissues seem to suffer loss of efficiency at a greatly accelerated rate. Youthful characteristics quickly disappear, the termination of the period of fertility is early reached, and signs of senility such as thinness of hair, lack of luster of the hair, changes in the texture of the skin, and instability of the nervous system appear.

405. **A Striking Parallel Between Human Experience and the History of our Animals on Similar Diets.**—There is perhaps nothing more worthy of careful consideration as a human problem than the suggestive results of the behavior of our experimental rats as modified by diet. They have varied from the most highly satisfactory type for the promotion of growth, fertility and the preservation of vigor, to the opposite extreme when little or no growth could take place and physical deterioration developed apace leading to early death. The well nourished rat is large and muscular and has a glossy coat, bright eyes and a quiet disposition. When placed in new surroundings it shows a strong desire to explore its environment. As soon as this is done it settles down to rest, and at no time, so long as it remains on familiar ground, does it manifest much activity. Its nervous system is stable and its threshold of stimulus relatively high. It is not apprehensive of danger and does not manifest much curiosity as to its surroundings except when placed upon new territory. Such a rat may be handled several times a week by lifting it by the tail by means of tongs, which causes some discomfort, yet it will fail to remember the experience or develop as a result fear or resentment at being handled in the same manner or with the unprotected hand. A cage containing half a dozen such animals can be opened without causing them to rise from a resting posture, and one can reach in with a bare hand and take them by the tails, pulling them about so as to collect the entire group in one hand, and can withdraw them as a single handful and demonstrate them to a visitor with their heads down for several seconds without causing them any alarm. They do not resent being handled, even being held suspended with their heads down, although this causes them some discomfort, and they do not attempt to bite.

406. **Nervousness of Animals on Certain Types of Faulty Diets.**—On the other hand, when the diet is faulty in certain respects, the nervous system is profoundly affected. This is perhaps most pronounced with diets deficient in calcium or in phosphorus. Inadequacy of the protein of the diet is also capa-

ble of causing irritability and nervousness. We have observed a group of rats which had been restricted during growth, to a diet in which the sole protein content was 6 per cent, half of which was derived from maize and half from peas. They were very apprehensive of danger and would retire in alarm when the cage was opened. Well nourished animals do not become alarmed under such conditions.

In extreme cases, young rats which are restricted for a few weeks to such deficient diets become extremely nervous and irritable. When the cage is opened they may retreat as far as possible and sit upon their haunches or crouch in an attitude betraying great alarm, and squeal when an attempt is made to pick them up with tongs. One would certainly be bitten if one were so rash as to attempt to take them in the bare hands. It is often difficult to seize them by a foot or by the tail by means of tongs because of their frantic springing about. They even leap out of the cage past their would-be captors. Normally nourished rats can be placed in a box together and transported to the balance for weighing, without arousing any excitement. When the box is temporarily uncovered they do not evince a desire to escape. The nervous ones, made timid by faulty nutrition, under these circumstances jump about frantically and make violent efforts to escape the instant that a ray of light is admitted to the box. Not infrequently we have corrected the diets of animals in this condition of nervous instability and have been able within three or four weeks, to pick up the entire group of five or six with one bare hand without causing them any unrest.

There are in our experience all gradations of nervous instability between these extremes. Some behave so as to cause an entry in the note-book that they are "wild," but never reach an extreme degree of timidity. Many times we have observed young rats nourished by mothers whose diets were deficient in calcium, to develop typical symptoms of tetany. They would appear to be well nourished up to the seventeenth or eighteenth day of nursing, then would suddenly develop a paroxysm. These seizures were experienced at intervals for some hours when death resulted. Timidity and nervousness are also characteristic of many rats whose diets are deficient in the antineuritic substance.

407. **Tetanic Seizures in Young, Nursing Mothers Whose Diets Are Faulty in Certain Ways.**—In this connection mention should be made of the frequent destruction of young rats by

their mothers. There are two general causes of infant mortality in our colony. In one case the mother reacts normally toward her young and makes an effort to nurse them, but fails to do so successfully because of errors in her diet which prevent the secretion of milk of a normal character. Under such conditions the young may grow for a time, then become stunted and require a much longer period of dependence upon the mother than is usual, but finally reaching a state of maturity where they are capable of subsisting on the diet of the mother. Again under other experimental conditions, especially when the diet of the mother is deficient in calcium, the young may grow in a manner essentially normal until the fifteenth to the eighteenth day, or thereabouts, and then develop tetanic spasms, strikingly suggestive of tetany in infants. A pathological state different from that just described, but characterized by great excitement, and seizures in which the young sit up on the haunches and squeal violently, is frequently seen in little rats which are nursing mothers whose diets are deficient in water-soluble B, and appears to simulate infantile beri-beri. Once little rats are observed to have attacks of the kinds described, they usually die within a day or two.

408. **Infanticidal Tendencies in Nursing Mothers Caused by Faulty Diet.**—In another class is to be placed the mother rats which destroy their young within a day or two after birth. This, we have found to be the rule in animals which are restricted to diets in which the protein moiety is inadequate, especially when it is of rather poor quality and constitutes but a small percentage of the food mixture. This tendency to infanticide may be, therefore, the specific result of semi-starvation for amino-acids. The nature of the lesions which develop in young rats which are suckled by mothers on faulty diets of the characters described above have not been sufficiently studied to warrant any detailed discussion of them.

409. **Changes in Our Basis of Judgment Regarding Criteria of Quality in Diet.**—The foregoing account of the changes in the viewpoint with which we have come to regard nutrition and the interpretation of its problems, shows clearly the physiological necessity for a proper balancing of the diet in a sense different from that in which the term balanced was employed in former years. Then it was used to express the ratio between the protein and other energy yielding constituents of the food mixture. Now it includes fine adjustments in the relative pro-

portions in which the products of protein digestion are furnished by the diet, the concentrations of the several inorganic elements which it contains, and the abundance which it affords of the essential vitamins.

410. **The Diet Should Be as Near the Optimum as Possible with Respect to Every Factor.**—The object of this account of the effects of faulty diets which fall short of meeting the nutritive needs of the body only to minor degrees, and in many cases in respect to factors which are not primarily concerned with the production of the "deficiency" diseases, is to emphasize the importance of taking regularly, a diet which approximates closely the optimum with respect to every component. Whenever a diet, which deviates much from the optimum in its constitution with respect to any of its parts, is adhered to for any considerable period, it leaves its mark upon the organism, and causes its deterioration at a rate faster than would result under more favorable conditions.

411. **Optimal Physical Development and the Prevention of Illness, the Present-Day Objective.**—Until recently the medical profession was interested exclusively in the sick. The well baby, the well child or the well adult, were entirely neglected. Now the idea is gaining ground that it is more important to keep a person well than to cure an illness after it has developed. This is the great ideal of preventive medicine. But just as in the past the baby was regarded as well until midnight wails, prostration, or a terrifying rash or eruption made attention to its condition imperative, so to-day physicians, health officials and the public itself, are in great measure ignoring all except the most spectacular and compelling alarms in health matters. Epidemics have forced the chlorination of water supplies and the enforcement of quarantine. The effects of unwise selection of food can confidently be asserted to exercise a greater debilitating effect upon an individual than does in many cases an attack of an acute infection in a well nourished one. Yet the effects of faulty nutrition exhibited by more than half the people around us attract little or no attention.

412. **Possibilities of Scientific Nutrition Not Generally Appreciated.**—We hear much of clinics for the removal of diseased tonsils and adenoids, and for the repair of defective teeth, but almost nothing of a fundamental nature about the adoption of habits of living which would in great measure exempt the next generation from these physical burdens. Partial physiological

exhaustion as exemplified in chronic constipation, hypersensitiveness of the nervous system, diabetes and kidney lesions has become so common that they attract little attention except from the patient and his physician, yet there is much reason for belief that a more rational system of living, prominent in which would be a wise choice of foods, would in great measure cause the disappearance of these debilitating conditions.

The trouble seems to be that we are still retaining habits of thought which must sooner or later become antiquated. Case reports, autopsies and histological studies still focus our attention upon the nature of the lesion, its accurate description, and its differentiation from other conditions. Bacteriological studies and the triumphs of the serologist in immunization against infectious disease, hold most of our attention, while the physiology of normal conditions, receives but little consideration. Without minimizing the importance of pathology, bacteriology and parasitology in contributing to human health and comfort, it may well be asserted that the time has arrived when greater attention should be given to the most fundamental problem of all, viz.: *the supervision of the conditions under which the normal development of the individual takes place. An effort must be made to perfect the environment so as to make the many structures of the body function in a manner which approximates the physiological ideal.* Such an attitude toward health matters would necessitate the recognition as of paramount importance for the realization of its aims, the optimal regulation of the chemical medium by which the tissues grow and are sustained. Technical studies have brought to light what casual inspection failed to discern, that our most effective defensive barriers against most of the dangers to which our environment exposes us lie within us. Perfection of physiological development, and the preservation unimpaired of the functions of the organs and tissues of the body assure, in great measure, immunity against the painful effects of certain diseased conditions. Among all the hygienic factors which influence the welfare of human beings or the lower animals, the nutritional factor stands first in importance. It is hoped that the illustrations presented of the manner in which the diet may be selected so as to form a great bulwark in the protection of vitality are sufficiently convincing to lead to a better appreciation of this much neglected agency for the promotion of health.

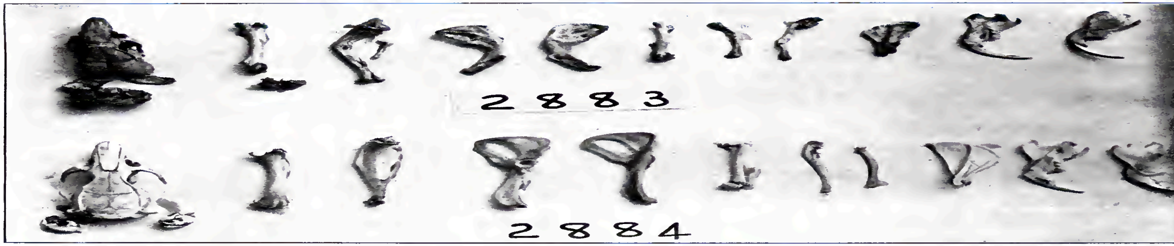

Fig. 19.—Illustrates the marked difference in the quality of the skeleton of rats which were fed on diets which were poor and good respectively. The bones at the top (Lot 2883) are those of an animal whose diet was satisfactory except that it was too poor in calcium. Note the dark coloration due to hemorrhage; the detachment of the head from the femur; the separation of the bones of the skull; the deformity of the pelvic bones; the crooked form of the radius and ulna; the inferior development of the scapula and the failure of the bone of the mandible to grow out around the base of the incisors as far as it should. Note also that these incisors are growing at a wrong angle and are too long and poorly formed.

Rat 2884 took the same diet as the above but with calcium carbonate added. Its bones were much lighter in color, and were dense and well formed.

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CHAPTER XVII

THE DIETARY HABITS OF MAN IN SEVERAL PARTS OF THE WORLD

413. **The Polyphemic Eye of the Faddist in Diet.**—From what has been said in earlier chapters it will be readily understood that students of nutrition during any period previous to the last five or six years must necessarily have had an inadequate understanding of the fundamental principles which underlie the science, and hence were unable to interpret correctly their observations. Several writers were inspired with enthusiasm for a special type of diet and each had, therefore, a polyphemic eye for one or another nutrient principle as overshadowing others in importance. Thus Crichton-Browne (1) had the conviction that meat eating promotes not only physical vigor, but is responsible for many other manly attributes as well. Chittenden (2) was an earnest supporter of the theory that a low protein dietary best promoted physical and mental well-being, while McKay (3) was led by his observations on the peoples of India, to the conclusion that a liberal supply of protein in the food of man was a factor of great importance in determining the success of the human dietary. It is now apparent that the protein moiety is but one of several indispensable components of an adequate food mixture, all of which are indispensable and must be viewed as of approximately equal importance. For each of these components there is an optimum, either of amount or constitution, which will best meet the nutritive needs of a mammal. We are now in a position to reëxamine, with a broader viewpoint than the earlier investigators, the whole subject of human nutrition in the light of the results of animal experimentation, with the prospect of arriving at a decision as to the best type or types of diets suited to the development of an imperial race.

414. **The Keynote to Successful Nutrition Is the Proper Selection of Food.**—It has been shown what chemical constituents form a satisfactory diet for a mammal and the experimental evidence upon which the accepted views rest has been described.

The dietary properties of each of our more important agricultural products and of each of the animal products serving as food for man have been pointed out. Emphasis has been laid upon the manner and extent to which foods which are, individually deficient in one or more respects tend, when combined, to correct each other's deficiencies. The evidence is overwhelming that the keynote to successful nutrition is the selection of foods having unlike dietary properties, but so constituted as to supplement each other's deficiencies and to make a mixture which affords the most satisfactory amounts of each of the essential food elements, rightly combined. The generalization has been made that a diet may afford a surprisingly great variety of food-stuffs, including cereal grains, tubers, fleshy roots, fruits, and liberal additions of muscle meats, and still fall far short of being adequate for the support of growth or for the maintenance of health in the adult. In the present chapter, the types of diets which are successful in a rather high degree will be described, and their effects on man and animals will be illustrated. At the same time the errors in the selection of food which mark the habits of a number of groups of people in different parts of the world, will be pointed out.

415. **Observations which Became the Basis of Important Deductions.**—The facts brought out by laborious experimentation are so well illustrated by human and animal experience in general, that it seems remarkable that so many physiologists and students of nutrition failed for such a long time to observe the evidence and to give it proper interpretation. Experience at the Wisconsin Experiment Station afforded the author an opportunity to contrast the superior growth and health of swine fed on satisfactory rations, with the poor growth in the scrawny, stiff-legged creatures so often seen on farms where the owners had not learned that it is not possible to keep a pig in a dry lot and feed it on grain, without resulting failure in pork production. It was at that time known to many shrewd animal husbandrymen that there are but two methods for feeding swine for profitable results. One was to feed the grain grown on the farm while the animals were running on a good pasture such as a clover or alfalfa field may furnish. The other was to feed the grain supplemented with liberal amounts of skimmed milk. A combination of these two plans leads to still better results.

While the investigations were in progress which have led to our present understanding of the science of nutrition, observa-

tions such as those emphasizing the inadequacy of diets consisting solely of vegetable products, the functions of which are those of storage organs, caused me to inquire into the dietary habits of man and animals with a view to finding, especially what relatively simple diets, composed of but one or a few articles, were at least reasonably successful in promoting well-being. Such an investigation into data which Nature presents for contemplation, revealed at once three important facts, which serve as the guiding principles upon which the experimental data since accumulated have been interpreted.

416. Many Instances of Successful Carnivorous Nutrition. —One of these facts, abundantly substantiated by common observation, is that there are many examples of animals subsisting entirely upon food derived from the tissues of other animals. The wolf, lion and tiger are familiar examples among mammals, and the eagle, owl and vulture are examples among birds. Nowhere do we find more remarkable physical development than among this class of animals. It is obvious, therefore, that the tissues of one animal contain everything which is essential for the nutrition of another. Those who accepted the old ideas regarding the necessary components of an adequate diet saw no reason for distinguishing between different types of carnivorous diets. Actually there are decided differences in the dietary properties of muscle meats as contrasted with the glandular tissues. Muscle meats are very similar in their dietary properties to the cereal grains, and in order to make them complete it is necessary to supplement them with respect to calcium, sodium chlorid and all three of the uncharacterized "vitamins" associated with the causation of the deficiency diseases. The flesh-eating of the carnivorous animals is a very different thing from that of civilized people in the temperate zones. For some unknown reason the latter have developed a special liking for muscle cuts of meat, as steaks, chops, etc., whereas the carnivorous among men and animals eat blood, glandular structures and bone marrow, fat and an appreciable amount of bone substance in preference to muscle tissue. Miss Simmonds and the author have found that suitable proportions of these tissues form very satisfactory diets for the rat, just as they do for the wild carnivora. Most people in the past have been satisfied with inaccurate and incomplete descriptions of food habits. With the greater knowledge we now possess, it is necessary to be more specific and accurate in all discussions of nutrition and diet (4).

417. Other Tissues Make Good the Deficiencies of Muscle Tissue in Carnivorous Feeding.—The deficiencies of muscle meats are entirely made good by the addition of blood which furnishes the common salt which is nearly lacking in muscle, and by such glandular organs as liver, kidney, etc., which furnish a relative abundance of all three of the uncharacterized dietary factors, the anti-ophthalmic, anti-neuritic and anti-scorbutic substances. Bone furnishes calcium which is not abundant in any other tissues of the body. All carnivorous animals appear to be partial to fat rather than protein as a source of energy and take large amounts of the latter when it is available. The most satisfactory carnivorous diet would appear to be such as is chosen instinctively by the Eskimos and polar carnivoræ. All of these as well as those of the cat and dog and rodent families seem to follow the practice of opening the large veins of the neck, when they have killed an animal, and lap the blood as long as it flows. They then open the abdominal cavity and eat of the organs and only after these morsels have been disposed of do they take muscle tissue. It is well known that carnivorous animals have the habit of finishing a repast by leisurely gnawing a bone. Thus they secure a properly balanced diet through selecting parts of their victims which have special dietary properties.

418. Several Examples of Successful Carnivorous Nutrition in Man.—There are several examples of strictly carnivorous nutrition in man in which the success attained is about as great as that seen in animals on similar diets. Thus the Eskimo, while a small people, are vigorous and capable of considerable exertion. There are climatic factors which may perhaps be regarded as a handicap to their well-being, but it is not easy to evaluate these, for the animals of the Arctic regions and the Eskimos as well appear to be thoroughly acclimated and to suffer little from low temperatures or lack of sunlight over long periods.

The American Indians who inhabited the plains east of the Rocky Mountains and subsisted upon the bison, were likewise a strictly carnivorous people during the greater part of the year. The cultivated products and wild fruits and berries formed at best but a slight variation from the monotonous flesh food supply. Lewis and Clark, Parkman and other reliable observers, testify to their being, in many instances, fine examples of physical development. Like the Eskimos they ate the entire edible part of the animals which served them as food. They did not even discard blood or the alimentary tract.

419. Lesson from the Health Experience of the Non-Citizen Indians.—There is no better illustration of the soundness of the views regarding the types of diets which succeed in inducing good nutrition, and the importance of selecting foods so as to produce combinations which are satisfactory for the maintenance of well-being, than the experience of the non-citizen Indian of the United States. All who observed the Indians in their primitive state, agree that most of them were exceptional specimens of physical development. During two generations they have deteriorated, physically, with few exceptions, in a manner more marked than has the last generation of Americans of European stock. The reason for this is brought to light through a consideration of the kind of food to which they have restricted themselves for years past.

There is no group of people anywhere having a higher incidence of tuberculosis than the non-citizen Indians. Wards of the Government, they have been provided with money and land, but have in general shown no interest in agriculture. Under such conditions most of them have lived in idleness and have derived their food supplies from the agency stores. In addition to meats, they have, therefore, for two decades or more, taken large amounts of milled cereal products, syrup and molasses, and canned foods, such as beans, peas, corn, etc. In other words, they have come to subsist essentially upon a milled cereal, tuber and meat diet. On such a regimen their teeth have rapidly become inferior, and badly decayed, and they suffer much from rheumatism and other troubles which result from invasion of the blood stream through infected teeth. Faulty dietary habits are in great measure to be incriminated for their susceptibility to tuberculosis.

Other classes of Indians who have become successful farmers, have not deteriorated as a result of contact with civilization, except in so far as they have suffered from alcohol and venereal infections. The non-citizen Indian has suffered most, not because of contact with civilization, but because of a detail in connection with that event, which can easily be remedied. He has suffered little if any more than white people living under similar conditions would have done, and indeed are actually doing today in many places.

420. Has Natural Vigor Anything to Do with Susceptibility to Tuberculosis?—There are many who doubt whether faulty diet has anything to do with susceptibility to tuberculosis, but

there is little doubt that it may be so. Experience has shown that there is no more effective therapeutic measure than proper feeding to raise the recuperative power of the patient. If such treatment affords greater prospect for throwing off the disease once it is established, it would be decidedly paradoxical to maintain that highly satisfactory nutrition could play no important rôle in protecting the individual against the establishment of the infection. Appleton has pointed out that the men of Labrador and Newfoundland suffer greatly from tuberculosis, although they spend at least half of the year out of doors in an invigorating climate. She states that owing to the strong winds which blow almost constantly during the winter, the houses are ventilated so thoroughly as to make garments wave which are hanging in the rooms for drying. She suggests that the faulty diet is the predisposing cause rather than unhygienic housing.

421. **The Food of the Lapps.**—An excellent example of the success of a strictly carnivorous diet in man, are the Lapps. These people are scattered throughout northern Scandinavia and the Murman coast and live almost entirely upon their reindeer herds and on fish. They eat not only meat, fish and fowl, and eggs of wild birds in summer, but secure a fairly large amount of milk from their reindeer. They are a short and heavily made people, with good physical development and great physical endurance. Like the Eskimo, they must exert themselves greatly at times in order to maintain themselves in their inhospitable land.

422. **Attitude of the Carnivora Toward Physical Activity.**—It appears that the carnivorous peoples have much the same attitude toward physical exertion as have carnivorous animals. When well fed they are lethargic and remain idle, or do work that requires little exertion. They bestir themselves only when pressed by hunger to do so. Dr. Grenfel states that the Eskimo is an inferior fisherman and will catch one fish to a white man's ten. This, we may safely attribute, in part at least, to intoxication from poisons of bacterial origin, due to putrefaction of protein in the intestine.

423. **Metchnikoff's Views Regarding the Generation of Toxic Products in the Intestine from the Putrefaction of Protein Food.**—The idea made popular by Metchnikoff, that the body is injured by absorption of toxic substances formed in the intestine through the agency of putrefactive bacteria, rests upon evidence which can hardly be doubted. The beneficial effects

resulting from taking a liberal milk diet, especially milk which has been soured by the bacillus acidophilus, are attested by a great many people. A very striking illustration of the manner in which a diet consisting largely of animal tissues modifies the bacterial flora of the intestine, and influences the physical and psychical condition of animals, is given by Herter and Kendall (5). These investigators restricted monkeys to a diet of eggs, and cats to a diet of meat for one or two weeks. They then shifted suddenly to a diet of milk and glucose. Previous studies had shown that eggs or meat encourage the growth of putrefactive organisms in the alimentary tract, whereas milk and glucose stimulates the growth of fermentative and lactic acid-forming organisms, just as does a diet consisting solely of carbohydrates. After one or two weeks on the milk and glucose diet, the animals were returned to the eggs or meat, respectively. These intervals were found sufficiently long to change entirely the character of the bacterial flora of the intestine.

As the proteolytic or putrefying type of bacteria began to predominate, which occurred promptly after restricting the monkeys to eggs, the animals became sleepy and rested their heads upon their hands in a bowed position. They were stupid and responded slowly to external stimuli, took their food very deliberately and manifested little interest in their surroundings. Not infrequently after a hearty meal the animals would spend much time trying to bite the woodwork of the cage. The urine voided was of small volume and highly colored, and amounted to approximately half that produced from the milk-carbohydrate diet. As the protein-digesting bacteria became established, in the intestine the amount of products of putrefaction which appeared in the urine increased markedly.

When the animals were changed to the milk-glucose diet, both the psychical and physical attitude underwent a great change. They no longer held their heads in their hands, but assumed an erect posture and were alert and bright, and showed a keen interest in their surroundings. Their appetites became sharp and the food was consumed with more avidity. The eyes, which were dull and lusterless while on the egg diet, became bright. They no longer attempted to chew the woodwork of the cage. The products of putrefaction of protein almost disappeared from the urine. The evidence from human experience seems sufficient to warrant the conclusion that similar changes in the diet of man induce similar modification in the bacterial flora of the

intestinal tract. One may safely conclude that excessive consumption of meat, with but small and insignificant amounts of carbohydrates, tends to promote the generation of toxic substances which induce lethargy in both man and animals.

424. **Meat-Eating in America Is Very Different from Practices of the Carnivora.**—There is considerable misunderstanding as to the effects of taking liberal amounts of meat. The meat eating of the people of America and parts of Europe is largely confined to muscle cuts. It is to be regretted that excessive meat eaters very frequently derive the greater part of the remainder of their food supply from degerminated cereal products and tubers. Such diets are faulty in several respects. They tend to contribute to the early deterioration of the tissues, and for reasons quite apart from the amount of meat consumed. Results due to faulty diet are not infrequently attributed to the meat fraction, when in reality other components of the food supply may be said to contribute in an important degree to the bad effects observed. It frequently happens that the other food components fail to supplement the meat, and correct its deficiencies. Success has been attained with laboratory animals restricted to a diet of muscle meat supplemented with such substances as are necessary to make it a complete food. The good development and vigor of carnivorous animals lies in the choice of parts of their victims so as to make a satisfactory adjustment of the necessary food essentials. This success serves to illustrate a principle which must not be lost sight of in interpretation of the cause of nutritive disturbances. The diet must be considered as a whole, and an accurate estimate made as to the degree of completeness of every essential factor. *Since, in this country the term "high protein diet" is generally synonymous with "high meat diet," it will be seen that disturbances of nutrition believed to be referable to excessive protein ingestion, may well be due, not so much to the amount of protein eaten, but to failure to take a complete diet. Such a diet is only to be secured through the proper selection of foods which make good each other's deficiencies. It is the completeness of the diet rather than an unusual amount of some one factor which is the most important consideration.*

425. **The Teeth of the Carnivora Were Excellent.**—The teeth of the carnivorous animals and of carnivorous man were of excellent quality so long as they adhered to their primitive dietary habits. With the change to a new type of diet, such as

is now common in Europe and America, savage peoples and others who have modified their diet in a similar manner, there has resulted rapid deterioration of the teeth and caries have become common. The teeth of the primitive Eskimo were excellent. According to Stefánsson, there was no word for toothache in their language. To-day the younger generation of the Eskimo dwelling along the Arctic coast of Alaska have teeth as defective as those of children in the States. They have been brought up in great measure on foods such as are available in the grocery stores in the United States, viz.: on flour, sugar, molasses, muscle meats and fish. It is a far cry from such a diet to that of their forefathers, although this could be discovered only as the result of the accumulated data secured through animal experimentation.

426. **The Nutrition of the People of Iceland.**—A most interesting experience is that of the people of Iceland. The island was settled in the ninth century by colonists from Scandinavia and Ireland. The colonists took with them cattle and sheep, but no poultry. The latter were not introduced until about a century ago. Their diet was practically carnivorous in character for several hundred years. Since agriculture did not prove profitable, they subsisted on milk, mutton, fish, and in some parts of the island during the summer, eggs were added to the fare. Very little vegetable food was eaten. The health conditions on this regimen were good and dental caries were unknown until after about 1850. Stefánsson exhumed 96 skulls from a cemetery dating from the ninth to the thirteenth centuries and presented them to the Peabody Museum of Harvard University. These have been described by Hooton (6), who found that there were no evidences of caries in any of them. There were but three or four defective teeth in the entire series, and these had suffered mechanical injury. During the last half century the incidence of caries has steadily increased in Iceland, and apparently because of changes in the character of the diet. Everywhere in Europe and America during the last century the use of degerminated cereal products such as bolted wheat flour, degerminated corn-meal and polished rice has steadily increased, owing to the extension of commerce and the changed conditions with respect to the relative numbers of urban and rural population. Not only has the amount of cereal products consumed greatly increased, but the modern milling methods have greatly reduced their quality by removing the germ and the bran layer.

It is very suggestive that such diets as we are discussing as in use in recent years are so poor as to produce faulty teeth in experimental animals, and that the teeth of mankind have deteriorated so rapidly within the last century.

427. **The Diet of the Inhabitants of the Hebrides.**—A diet very similar to that used in Iceland has also long been customary in certain islands in the Hebrides. The only agricultural crops which are very successful are turnips and potatoes. Cattle are kept in sufficient numbers to give one or two cows to each family. Some oatmeal is available and forms a constant, though not an abundant constituent of the diet. Many of the men are engaged in fishing and the unsalable parts of the cod form a regular and prominent part of the food supply. Milk, cod heads stuffed with livers, turnips, potatoes and oatmeal constitute almost the sole food supply of the poor crofters. The health of the people is excellent except that the incidence of tuberculosis among the natives is high.

The susceptibility of these people to tuberculosis is due in great measure to the irritation of the lungs caused by constant breathing of the smoke of peat fires. Most of the houses are very primitive turf structures without windows, or with windows which are fixed. The roofs are thatched and are without chimneys. Peat fires are kept burning all day and most of the night, and the only means of exit for the smoke is through the thatch or through the doorway. This annoyance is tolerated because of the belief that the thatch, which is renewed annually and is applied to the land for fertilizer, is made more valuable by being saturated with the products of incomplete combustion of the peat. The cows are actually housed in one end of the house serving as the human habitation, and the manure is removed but once a year and placed directly on the land. The lungs are injured by the irritating smoke and this is believed to predispose them to tuberculosis.

428. **No Rickets Among the Children of the Island of Lewis in the Hebrides.**—Perhaps the most spectacular thing about the relation of the diet to health in the Island of Lewis in the Hebrides, is the condition of the infant population. The babies are rarely taken out of the dark and smoky houses, except for a few minutes at a time in bright weather, because of the numerous duties of the mothers. They are, however, universally nursed and by mothers who are taking a diet, which although unattractive to the American palate is quite satisfactory

for the maintenance of growth and of vigor in the child and adult, and for the secretion of milk by the lactating mother. The greater part of their diet is cod heads stuffed with a mixture of chopped livers and oatmeal, milk, eggs and tea, with rather limited amounts of oatmeal, bread, butter and potatoes. It is principally a carnivorous diet, and contains only adjuvants of vegetable origin. The infants are all free from rickets, which is so prevalent in England and Scotland as to constitute a national health problem. In fact, the infant mortality in this island is as low as anywhere in the British Isles. Although the mothers suffer from over exertion in agricultural labor and otherwise, their infants are far better nourished than are tens of thousands in America at the present time, whose mothers are living on diets rich in cereals, potatoes and muscle meats.

429. Good Nutrition Goes Far Toward Offsetting the Effects of Bad Hygienic Surroundings.—This illustrates in a very satisfactory manner a fact which has been many times demonstrated in animal husbandry experience, viz.: that very good results can be secured in physical development in young animals which are abundantly supplied with a satisfactory diet, even when the hygienic surroundings are bad. This is not a defence of poor sanitation, but affords a basis for comparison of the relative importance of diet and other factors which influence development and vitality. The same may be said of exercise as contrasted with diet. Young bulls are often given wholly inadequate opportunity for activity, yet on a highly satisfactory diet they develop into remarkably fine animals. Exercise is of course a very essential thing to perfect health and the long maintenance of vitality, but highly satisfactory nutritive conditions are capable of protecting young animals to a surprising degree against physical and hygienic handicaps.

430. The Rearing of Young Lions in Captivity.—Another illustration of how modifications of the diet which formerly would have seemed unimportant, may make a difference between failure and success in growth and development is afforded in the experience of those who have attempted to rear young carnivora in captivity. It was not possible until within recent years to rear young lions in zoos or circuses, but to-day this is being done successfully in several places. Formerly it was the custom to give lions a large bone with a quantity of muscle attached. The animals ate the muscle tissue and attempted to gnaw the bone, but this was too large and hard to permit them

to secure much of its substance. There was danger of choking on bones which might be splintered, or which could not be cracked, yet which were so large as to be swallowed with difficulty. They were, in other words, restricted too largely to muscle meat and to an inadequate amount of bone substance. Under these conditions young lions invariably developed rickets and had to be killed because they were so deformed as to be unfit for exhibition. Now it has been learned that the diet should consist of liver and other glandular organs, such bones as shoulder blades which are easily consumed, fat, and at intervals of a few days pigeons or rabbits, the entire carcasses of which can be eaten. Muscle tissue is fed rather sparingly. Under such management, it is easily possible to secure satisfactory nutrition in these animals. The reason why such a practice succeeds where the older one failed, is now understood in the light of our knowledge of the special dietary properties of each of the tissues of the animal body.

431. **The Carnivorous Diet May Be Highly Satisfactory.**—It will be readily appreciated from what has been said, that both in human and animal experience, the carnivorous diet, when properly selected, or the diet which is largely carnivorous but supplemented with moderate amounts of vegetable foods, may prove highly satisfactory for the promotion of growth and the maintenance of vigor and longevity.

432. **The Oriental Diet.**—We may next consider a type of diet which has served to nourish more than half of the human race from time immemorial, and is still depended upon by more than half of mankind. This type is that used so extensively in China, Japan, the Philippines and elsewhere in the Orient. In it the vegetative parts of plants, the leaves, form a very prominent part of the food supply.

433. **Many Examples of Successful Nutrition Among Leaf Eating Animals.**—One of the three facts which stood out prominently in my consideration of the types of diets which had succeeded in human experience and with animals, was that certain peoples and many animals were thriving on diets in which the leaves of plants were important articles of food. Thus the grazing animals may live throughout their lives on grass or other palatable forage plants. All the animals of the cattle, horse, sheep, goat, deer and other types, in their early history had no grain, and subsisted entirely upon grass. The bison never had anything else throughout life. The giraffe feeds upon

the leaves of trees and shrubs. This idea seemed very fertile, when one considered that swine had, in our experimental trials, failed so signally in their nutrition when confined to a diet of a cereal grain or mixture of several cereals such as wheat, maize or oats. On reflection, it naturally occurred to me to consider the function of the seed as contrasted with the leaf. The former is a storage tissue, formed to supply the plantlet which develops during germination, with sufficient nutriment to enable it to form a root and leaf system. After this stage it is independent of further aid, and can secure everything it needs from the soil and air. The nutritive needs of a plant are very different from those of an animal. The plant can synthesize its proteins and carbohydrates as well as all the other components of its complex structure. The animal must secure these ready formed or it will perish. The leaf, on the other hand, is the laboratory of the plant. It is here that the numerous complex organic syntheses take place. We may reasonably assume that there are structures and chemical substances here which would not be found, at least in abundance in a seed. Were not the dietary properties of the leaf superior to those of the seed? Experimental trials showed clearly that this surmise was correct.

434. **There Are No Strictly Vegetarian Peoples in the Sense That Animals Are.**—There are no strictly vegetarian peoples in the sense that certain animals are. The human alimentary tract is not sufficiently capacious to admit of eating liberally of coarse herbage. There are a considerable number of people in the Orient who take very liberal amounts of green leafy vegetables as a supplement to a diet which is otherwise unsatisfactory and is much like that in use by many people in the United States. The diet referred to is one consisting principally of cereal grains, legume seeds, tubers and fleshy roots, and meats. Fish, eggs and poultry are eaten in varying amounts, but the outstanding feature of their diet is the large amount of green leafy vegetables which enter into it. This type of diet may be an excellent one, but it is probable that in human experience this is rarely realized. The people of the north of China, especially in the Shantung peninsula, are frequently fine specimens of physical development. Thousands of these were brought to France as laborers during the war. In this part of the country wheat is eaten largely instead of rice, and the entire grain is eaten. Further south more rice enters into the diet, and owing to a peculiar and baseless notion of its superior attractive-

ness, polished rice is preferred. This, it has already been pointed out, is very inferior in its dietary properties to unpolished rice. These and other factors which may vary from time to time, and which, a few years ago would have been regarded as of no significance, actually may be very important in determining the quality of the diet. At best, it is a diet which is sufficient, but in which there is little margin of safety. The special rôle of the leafy vegetables which it contains is to increase the calcium content and the fat-soluble A content of the food supply. Where eggs are eaten freely these supplement the food well with respect to the latter substance.

435. **The Importance of Certain Articles in the Oriental Diet.**—It can be readily appreciated that moderate variations in the amounts of leafy structures eaten, the amounts of eggs, and the extent to which polished rice enters into the diet in place of whole rice or other cereal grain, will have a most important bearing upon whether the diets of this type suffice for the maintenance of well-being. These variable factors will also determine whether there is an excess of any of the several factors in the diet, over the minimum on which a child can grow up and live what is ordinarily regarded as an average span of life. When a diet fulfils these conditions it passes as satisfactory, but there is good reason now, because of the results of the experimental studies of the last few years, to question whether any diet is as satisfactory as it is possible to make it. The final goal is to strive to discover whether any dietary regimen in use by man best promotes his vitality to the maximum. There is good reason to believe that the Oriental diet of the type under discussion, is at best, but a second rate one, and that it is not capable of meeting the needs of the growing child except in special cases where the most fortunate selection of articles is made. It does not, in general, support vigorous health and stimulate effort to an advanced age.

436. **No Foods in China and Other Oriental Countries Suitable for Feeding Young Children.**—It is certainly true that the diet of China, Japan and other countries in which the same general habits prevail, is not suited for the proper nutrition of young children. It has always been the practice of mothers there to nurse their infants for very long periods, even four or five years being not unusual. The early weaning of infants which is so widely practised in Europe and America, is made possible because of the availability of an abundance of milk of

the cow and goat. If the Orientals weaned their children at nine to twelve months of age as is the custom in this country, their infant mortality would be very great, for their foods are not suitable for feeding to young children and older infants.

In certain respects this is to the advantage of the Oriental infants but in others it is a disadvantage. Thus, since the mothers are, in general taking diets which are sufficient to meet their bodily needs in a fairly satisfactory manner over a considerable number of years, they are able to secrete milk of moderately good quality and for many months or even for several years. Their infants are, therefore, protected against the intestinal disturbances which are so frequently the result of feeding milk which is in bad bacteriological condition in this country. They likewise fail to suffer from rickets as do a large number of children in Europe and America. Their mother's milk or that of a wet nurse is the most appropriate food for them, and they in general during the nursing period, but no longer, fare better than do those children in our country whose mothers are limiting their diets largely to bolted wheat flour and other degerminated cereal products, potatoes and muscle meats, the meat, bread and potato type of diet. On this they are unable to secrete milk of good quality and after a few weeks or months their milk supply falls off or becomes of poor quality and weaning becomes imperative.

437. **Difficult to Maintain Normal Nutrition in the Child After Weaning.**—After weaning, however, it appears that the diet of the Oriental child is ordinarily less satisfactory than that of the American or European child. This is due in great measure to the lack of milk, of which the Chinese, Japanese and Filipinos have never had a supply until within recent years when canned milks have been introduced. There is some definite evidence to which one can point in support of this view. Fifteen years ago there was a great influx of "picture brides" from Japan into California and other Pacific coast cities. We have, therefore, a large number of children in this country of Japanese parentage. Both boys and girls are larger at all ages than are Japanese children born and reared in Japan (7). Who would doubt that it is the superior food which they receive which makes them outgrow their relatives across the ocean? The Chinese are smaller in the south than they are in the north, where wheat and millet replace rice in the diet. In southern China polished rice is the most desired cereal. This use of a

degerminated and decorticated cereal makes a very important difference in the satisfactoriness of the mineral content of their diet, and is probably sufficient to account for their relative physical inferiority as compared with their northern neighbors. There is but one explanation for their liking for polished rice, and that is custom. Polished rice is inferior in every respect to the unpolished grain, but since it is fashionable to eat the former kind, those whose diet is much simpler, as is for example the poor laborers, who derive their sustenance largely from rice and fish and a few vegetables, take pride in feeling that, however hard their lot may be in other respects, their rice is as white as their more fortunate neighbors'. The ease with which a firm and established demand for bolted flour, polished rice and other degerminated cereal products has been created through advertising, shows how unsafe is appetite as a guide to the selection of food.

438. **Heredity Versus Nutrition as a Factor Determining the Size of a People.**—The question has been raised on several occasions when the size of a people has been mentioned in connection with the nature of their food, whether size is not entirely a racial characteristic, and is inherited, rather than being determined by such agencies as nutrition. It seems to me that we have some very good evidence on this point in the histories of our rat families described in the preceding chapter. When the nutrition of these animals fell just under a certain standard, there was no easily observable sign of malnutrition, their appearance and fertility remaining such that they would be judged by anyone to be "normal," yet the size diminished from generation to generation. This is not, of course, set forth as an inheritance of an acquired character, but only as evidence that physically inferior parents tend to pass on their defective constitution to their offspring. The prompt increase in size of Japanese children born in California and fed upon the products of its farms, over the sizes characteristic of children of the same ages in Japan, would seem to harmonize well with the view which we have come to hold concerning the quality of the Oriental diet. Horses introduced into the Shetland and Orkney Islands have degenerated in size and that size is inherited in their offspring. Here again we see the effects of such a scanty and somewhat inadequate food supply that the animals are stunted in their growth. Perhaps it is more accurate to say that their food supply is sufficiently scant and precarious in the

winter season to interfere with their growth, and that their small size is due to permanent stunting from periodic starvation through several generations. The inferior physical development of these horses to-day must be admitted, and is certainly not due in any great measure to artificial selection. In another region of the world where pasturage is abundant throughout the year, there is every probability that the size of these animals would increase.

439. The Climate of California Not so Stimulating as That of Japan.—According to Huntington, the climate of California as a whole is less stimulating than is that of Japan, and is, therefore, less satisfactory from the physiological standpoint (8). He bases this belief on the results of his studies which show that wherever the climate has a favorable range of temperature change from day to night, and is characterized by storminess of the cyclonic type, there the people show energy and aggressiveness. Japan, in respect to its storminess ranks as one of the most stimulating regions of the world. It seems remarkable that a very favorable climate, which all would doubtless agree Japan has, should, be less favorable to the growth of its children than a less stimulating climate, if there were not another factor at least operating which is less favorable in Japan than in America. That this factor is the diet, there can be little room for doubt, since in several generations a diet of the type there in common use would effect a decrease in the size of animals restricted to it.

440. Greater Danger in a Simple and Monotonous Diet Than in a Varied One.—It is true of any people, that those with means live in better houses and have a more varied and abundant food supply than do the less prosperous part of the population. The poorer classes among Orientals, as in Western nations, live, generally speaking, on a simpler diet than the well-to-do. While it is true that simplicity in diet is perfectly safe and satisfactory provided the food is wisely chosen, there is more danger that a food supply which is monotonous and contains but few articles, will be sufficiently poor to make its effects clinically recognizable, than would be the case if the food offered greater variety. This might be true even though the faults in the diet were of the same magnitude as those of the simpler one, for in the former case the frequent changes in menus would cause an alternation of the factors which depart from the normal, whereas in the latter case the same factors would tend to

be faulty over a long period and their effects would be cumulative and would accordingly do more damage.

It is for the reason just stated that the poorer classes in several parts of the world suffer from beri-beri. Any people having a relatively high incidence of any deficiency disease, are certainly to be regarded as a group all members of which, so far as they subsist upon a similar type of diet, are borderline cases of malnutrition whether or not they show any clinically recognizable signs of disease. There is good reason to believe that the Japanese people can become larger and more powerful physically if they can institute certain changes in the character of their diet.

441. **Importance of Milk in the Diet of Western Nations and of Pastoral Peoples.**—The third fact which became clear in connection with the examination of the dietary practices of man and animals, was that diets which were derived from miscellaneous sources such as cereal grains, legume seeds, tubers, fleshy roots, with or without meats, but supplemented with liberal amounts of milk, sufficed to maintain satisfactory growth and marked vigor. Animal husbandry experience afforded strong evidence of the excellence of milk as food for growing animals, but especially of its high value for supplementing other foods such as the cereals in pork production. It was recognized generally, that the two best methods for promoting growth in swine were, either to combine milk production with a creamery, so that the skim milk could be returned to the farm and fed to hogs as a supplement to corn, or to feed the grain raised on the farm to hogs which were supplied a good pasture. The explanation of the cause of success of either of these practices was not understood, but we now appreciate the unique significance of the value of the mineral content and the fat-soluble A content, as well as of the supplementary value of the proteins of the leaves of our best forage plants, and of milk, in making good the deficiencies of the grains in these factors. The great value of skim milk in pork production made it very desirable to find a substitute for milk in the rearing of calves, and much effort has been expended in several of the Agricultural Experiment Stations in America to find a calf feed which was derived from foods other than milk which would prove wholly satisfactory. The results of these efforts have supported the view that there is no effective substitute for milk.

442. **The Vigor of Pastoral Nomads.**—When we turn to

human experience with diets rich in milk, some most interesting observations are met with. Certain regions have throughout history, produced vigorous and aggressive people. The Aryans and Mongols developed in the high pasture lands of Central Asia, where agriculture did not yield a return for labor, and where the care of flocks and herds formed the chief means of subsistence. Here in a climate characterized by extremes of heat and cold and of drought have originated the virile peoples who have become the possessors of the lands in every direction where the climate and soil were more favorable to an easy existence. Abstemious nomads, who knew no indulgence, and were every few years brought to face disaster through a scantier rainfall than usual, left their homes in wave after wave and dispossessed their neighbors in more favored lands. But in those more favorable circumstances where they came as conquerors, they not infrequently, in time degenerated into ease-loving agriculturists.

443. The Jews Were Originally Pastoral Nomads.—The migration of the Jews under the leadership of Abraham and Lot, from the dry plains of Mesopotamia, bringing their flocks and herds, and appropriating to their own use the better watered lands of Palestine, represents another example of the vigor and determination as well as manly qualities of other sorts, developed by a race of herdsmen. The Bedouins of Arabia and the Taureg tribes of the Sahara are other examples of peoples of great physical perfection and high mental attainments, subsisting under the most adverse conditions of climate and aridity, by converting a scanty pasturage into human food and clothing through the agency of their sheep, goats, camels and cattle.

Semple (9) has written an excellent account of the characteristics of the peoples of plains, steppes and deserts, as compared with other geographic environments. We need not judge their qualities entirely by our own standards. They are conceded to possess courage and hardihood and keen powers of observation. Their standards of honesty and respect for property rights depend on whether their relations are with one of their own people or with a stranger or foreigner, but this trait is in great measure the result of their environment. David, the self-reliant and brave youth, the great captain, and the national hero in whom all the noblest elements of Hebrew genius were combined, was the product of a shepherd tribe.

444. Diet an Important Factor in Determining the Physical

and Moral Attributes of Peoples.—Students of human history have many times attempted to discover the causes which have determined the peculiar traits of different peoples, but no general agreement has been reached as to the relative importance of racial stock, climate and geographic environment in determining physical, mental and moral attributes. Aside from a small group of sentimental enthusiasts who have discussed the merits of vegetarian practices as contrasted with meat eating, largely on the basis of whimsical evidence, and moral considerations, no one has, however, attributed any great importance to the character of the diet, except as regards abundance or scarcity of food, on the character and physical well-being of peoples. I would not detract in the slightest degree from the importance of inherited characters, or of physical environment as factors in the formation of human qualities, but must insist that students of mankind have hitherto failed to realize the importance of the selection of the food supply as an agency in the improvement of a race.

445. **The Arabs as an Example of Excellent Nutrition.**—The people inhabiting Central Asia domesticated animals of various kinds from which the domestic cow, sheep, goat, camel and horse have been developed through selection of certain types for breeding. Much of the country in that part of the world is too dry at times during the summer to make possible any reasonable degree of certainty of the outcome of the cultivation of crops, and is to-day largely tenanted by pastoral tribes. It was in the semi-arid regions of Asia that the earliest advances toward achievement were made. We see in certain of the pastoral Arab tribes to-day, people who are living much as have their ancestors and those of their neighbors, for hundreds of generations. The Arabs are physically as fine a people as any in the world. They are singularly free from physical defects, and present the ideal of physical beauty in a remarkable number of individuals who are not disfigured by the date boil or Aleppo button which is caused by an infection in the face, usually occurring during childhood. They live in a climate which is inhospitable a large part of the year because of excessively high temperatures. They have contended with drought and scanty pastures from time immemorial, yet they are a vigorous and virile people. Deformities are very rare among them, and their children do not suffer from skeletal abnormalities characteristic of rickets as do so large a proportion of those of Europe

and America. Not only are the Arabs well developed and athletic, but they have the courage to care for their flocks and herds under the most trying conditions. Actuated by the desire to trade or to carry on warfare, or stimulated by religious zeal to visit the holy cities of the Mahometans, they have undertaken long and tiresome voyages over the parched deserts. No people can have such a history, who have not had a diet which closely approached the optimal relations in respect to all its parts.

446. **The Diet of the Pastoral Arab.**—As would be expected, the diet of the pastoral Arabs consists in great measure of milk, supplemented with moderate amounts of meat, cereals and dates. In settled agricultural districts pomegranates, melons and a few other things enter regularly into the food supply. A great proportion of the wealth of Arabs consists of flocks of sheep and herds of goats and of camels. Cattle and horses are of secondary importance, because they are poor travellers. The milk used is derived from goats and camels and is mostly soured promptly and eaten as curds, because of the impossibility of preserving in a warm climate so perishable a food by other means. Cheese and dried curds are also staple articles of diet among them. This regimen represents a diet largely of a carnivorous nature, but supplemented with more or less of vegetable foods. It is of the greatest importance to these peoples that their diet does contain much milk for they have little opportunity to eat of the articles which are suited for the preparation of salads and greens. They could not subsist upon a meat, cereal and fruit diet without becoming inferior physically.

447. **High Protein Diet Is Excellent if Properly Selected.**—The relative merits of diets poor or rich in protein have been much discussed. The experience of the pastoral nomads of Arabia and other parts of Asia answer this question very definitely. A diet of milk and meat with small additions of vegetable foods is very rich in protein and it induces most excellent development and great longevity. According to the Encyclopedia Britannica (Vol. 2, p. 285, 11th Ed.), "physically the Arabs are one of the strongest and noblest races of the world." Baron de Larrey, surgeon-general to Napoleon on his expedition to Egypt and Syria, wrote: "Their physical structure is in all respects more perfect than that of Europeans; their organs of sense are exquisitely acute, their size above the average of men in general, their figure robust and elegant, their color brown;

their intelligence proportionate to their physical perfection, and without doubt superior, other things being equal, to that of other nations." In the same article it is further stated of the Arabs that "Simple and abstemious in their habits they often reach an extreme yet healthy old age; nor is it common among them for the faculties of the mind to give way sooner than those of the body."

The use of very liberal amounts of milk is the rule among the peoples of Northern Africa, Arabia, Mesopotamia, the Balkan States and throughout wide areas in Asia. Wherever dairy animals are abundant in proportion to the population, fine physical development is seen without exception.

448. **McKay's Observations on the Diet and Physical Efficiency of Hindu Peoples.**—McKay (3) has described the physical condition of the habitants of different parts of India, and correlated this with the character of their diets. His observations leave no room for doubt that the pastoral tribes are vastly superior in strength and health and manly qualities generally, to other classes of Indians. In those parts of India where the diet is largely derived from cereals the physical development of the people appears to be poorest. The rice eaters of Bengal are the most extreme example. The details regarding the components of the diets of the different classes studied by McKay are not sufficiently complete to serve our present purpose as well as we would wish, for he was interested primarily in the amount of protein which the different diets supplied. At the time his book was written, it had been hastily concluded by investigators that science had revealed all the facts necessary for the rational control of diet, and that it remained merely to determine certain minor principles which could contribute to physiological well-being. It was not deemed of importance in his elaborate investigation, therefore, to list the individual foodstuffs eaten and their quantitative relations. To-day this is regarded as the most essential thing to know, when we are called upon to evaluate a dietary regimen. McKay's studies, based upon personal observations, and on the reports of officers of the British Army to their Government concerning the fitness of the men in different parts of India for military service, forms one of the strongest confirmations of the applicability of the principles of nutrition discussed in this book to human experience.

The sour milks used so extensively throughout the East are variously designated sheneena, leben, yohourt, keffir, koumiss,

matzoon and dadhi, and are derived from milk of goats, camels, sheep, cows or mares. The fermentation is not purely a lactic acid formation through transformation of the milk sugar, but includes an alcoholic fermentation as well. All these sour milks contain not only a relatively high acidity due to lactic acid, but more or less alcohol as well.

449. **Relation of the Consumption of Dairy Products to Health in Parts of Europe.**—We can draw another parallel between large groups of people who show very marked differences in physical development, due, we believe, primarily to the differences in the quality of their diets. In Sweden in 1900 there was approximately one dairy cow to every two inhabitants. A similar relation is held in Switzerland with respect to the development of the dairy industry in relation to population. On the other hand the Southern United States had but one cow to five to ten or more people. There are no places in Europe where more hardy and aggressive men and women are to be found than in Scandinavia and in Switzerland. In marked contrast stand health conditions in the Southern States, as is shown, among other ways, in the high incidence of pellagra, which Goldberger has demonstrated, is directly attributable to inadequate diet. Like many other lines of evidence, we cannot push too far our contrasts of this character, because other factors can be readily suggested to account in a satisfactory manner for observed facts. Human subjects do not as a rule restrict themselves to one-sided diets to a degree which leads to unequivocal and extreme conditions corresponding with the results of animal experimentation. The parallels which we have drawn, do, however, correlate so well with the results of studies on animals as to leave little room for denial of their justification.

450. **Huntington's Views on the Effects of Climate on Man.**—Huntington believes that climate is the most important factor in determining the development of a highly progressive race or nation. As a result of his studies he concludes that a mean temperature of 64° F., a mean humidity of about 80 per cent, and frequent changes of temperature are the most desirable conditions for physical work. Statistical evidence is offered to support the theory that only people who live under conditions of relative storminess become industrious, capable and successful. His evidence is very convincing, yet as I read his books (8) on Civilization and Climate, and World Power and Evolution, I could not help forming the conclusion that while climate is un-

doubtedly a factor of great importance in determining well-being and consequent achievement, the author had ignored facts which modern research has brought to light in the field of nutrition, which should find a place in any discussion of human geography.

451. **Contrast of the Achievement of the People of Canada and Those of the Bahamas.**—We have already discussed the widespread occurrence of pellagra in the Southern States, and the apparently conclusive evidence that it is a disease of the poorly fed. Let us examine a contrast made by Huntington of the virility of the Canadians and the improvident, lazy natives of the Bahamas. It is stated that at the time of the Revolution certain Loyalists in the Northern States preferred to emigrate to Canada rather than live under the Stars and Stripes. Other Loyalists in the South betook themselves to the inviting climate of the Bahamas for a like reason. We will all agree that their ancestors were equally capable and aggressive, although of very different mental types. The former are, it is pointed out, an industrious, educated and progressive people, whereas the latter are indolent and unprogressive, having suffered retrogression since their settlement in the islands. The explanation offered for this great difference in quality of the two groups today, is that the climate of Lower Canada is a highly stimulating one, whereas that of the Bahamas is too mild and uniform.

While at first thought it seems logical to attribute the differences in stamina and aggressiveness of the Canadians and the people of the Bahamas to climate, there are now good reasons why we should consider other possible factors, notably the character of the diets of these two groups of people as a factor contributing to the success of the former and to the failure of the latter. Before discussing these differences it will be well to consider in some detail the part which may be played by climate and by diet on the physiological well-being of man. We shall, therefore, return again later to the part which the character of the food supply of these two geographically different regions has probably played in determining the attitude of their peoples toward life and work.

452. **Most People Are Unwell.**—No one will be likely to dispute the statement that most people are unwell, and that their failures, indiscretions, fits of temper, tendency to complain, tendency to give themselves up to reflecting on the possibilities for everything going wrong, their lack of enthusiasm

and other qualities which contribute to making them unhappy and inefficient creatures, are in great measure the result of ill health. We must grant that hereditary mental defects are widespread and are inherited as are other mental tendencies, but who can say how frequently the confirmed grouch is not what he is because of disturbances in his metabolic processes. The peevishness and unreasonableness of persons convalescing from serious diseases is a matter of common knowledge. Intolerance tends to develop in those who are continually in low spirits, and there can be no reasonable doubt that the diet may deviate from the optimal even in the United States, to a degree which can easily cause the results we see. It has produced comparable effects in our rat colony, when the choice of food was entirely comparable to human experience here.

Under faulty nutrition the machinery of the body tends to break down in places and with frequency. The exact nature of the defects which develop cannot in general be traced to their ultimate causes. Chemistry and histology have now made it clear that the functions of *living* matter depend solely upon the chemical complexes contained therein, and especially on the structure or organization, of its components. Its peculiar properties depend upon its structure. This is not homogeneous, but affords a wide variety of types which are revealed by histological methods. It is the minute structure of the protoplasm which suffers change when the nutritive conditions deviate from the optimal, and the result is faulty operation and an abnormal human being or animal. We have become well aware how very slight changes in the chemical or physical conditions may make pronounced differences in the properties of emulsions or of colloidal solutions. It has been demonstrated in our study of the effects of varying the ratios between calcium and phosphate in the diet on the histological picture of the bones, *that equally small deviations from the optimal composition of the food may in certain cases, produce profound changes in the manner of organization of the finer structures of the living tissues.* Function, too, has been shown to deviate to a degree comparable with the histological changes.

453. **The Most Stimulating Climates Are Not Promoting Health in Man More Than Less Stimulating Ones.**—If climate were responsible for health to the degree that its enthusiasts believe, how are we to account for the amount of sickness, early aging and physical inefficiency seen in the most favorable cli-

matic areas, such as the northeastern quarter of the United States and England, and the fine physical development of the Arabs and the pastoral tribes of Asia, whose climate is less stimulating? The teeth of the Americans and English of the present generation are indescribably bad, even where the climate is held to be best adapted to health, and to the promotion of physical and mental activity. What stands in the way of progress of Asiatic and African peoples which has kept them far behind the Europeans and Americans in advancing learning? It seems more plausible to regard the failure of certain peoples to progress as primarily a geographic one quite as much as climatic. The nature of the land, and its rainfall determine the character and vigor of the vegetation, and indirectly the character of the diet. Climate determines the kind of agriculture which is profitable, and, therefore, the most satisfactory mode of life of the people of any region. Conditions of living are often so hard that the vitality of every individual is taxed to the utmost to secure the primary physical needs for food, clothing and shelter. In the case of the herdsman his constant activity in the open denies him the opportunity to invent machinery or to develop experimental sciences. He never feels the need for these, because of his mode of life. Climate does not necessarily prevent his advance, except indirectly through determining his mode of life and the things upon which he will fix his thoughts. There is little prospect that an arid region can be utilized in any other manner than through raising animals on its scanty pasturage, so it seems impracticable to attempt to make anything out of such places except what they are. It is, however, quite another matter when we turn to tropical regions, with their unlimited possibilities for agriculture. Are we to accept the gloomy picture which Huntington draws for us of the utter hopelessness of making the tropics the abode of human culture? I am not convinced that this problem is an insolvable one.

454. **Plant and Animal Enemies in the Tropics Are More Serious Than Climate.**—Are not the real enemies to human life and happiness in the Torrid Zone, plants and animals rather than temperature and humidity? If this is admitted, no one who is imbued with the spirit of modern science, would seriously doubt that the improvement of conditions of living and of man himself in the warmer parts of the world is possible provided the solution of the problems is attempted in the right manner. As for the animal enemies the scientist will ask those who may

give him information: What are the peculiar habits of each species which we desire to rid ourselves of? What is their food and what is the history of their reproduction? Has each of them any natural enemies either animal or bacterial or fungal? When he has secured such information as is available, he sets himself to study in the minutest detail, every character which may enable him to overcome his enemy whether it be a serpent, worm or insect, and ultimately, as the result of the accumulation of data which seems dry and uninteresting to anyone but the specialist, he is able to control the pest or to exterminate it. When the human mind of a certain type is freed from interference, and is given resources, and a specific problem to solve, the result is practically a certainty.

When we turn to plant enemies, we find the tropics filled with them. Conditions for vegetable growth are so favorable that human strength cannot cope with them. But nowadays we do not regard it as necessary to struggle by means of living flesh with the weeds which seek to choke our useful plants. We harness and direct the forces of nature. There are abundant sources of energy available to relieve mankind entirely of the necessity of laboring with his hands. The energy of mountain torrents, of most of the large and small rivers, of the tides, of the winds, and of sunlight, are as yet very little utilized because the stores of fossil plant tissues in the form of coal have made it cheaper to use it prodigally rather than seek to compete with this source of energy in other directions. But who is so faint-hearted as to think that it cannot be that energy will be made available to turn the soil as often and work it as thoroughly as is necessary in order to eradicate the dragon of vegetable growth which discourages the would-be farmer of the tropics? I can see no great difficulty in the use of numbers of large lenses, cheap and relatively imperfect, for concentrating the sun's rays to several times their existing dispersal, and thus creating temperatures sufficient to destroy all existing vegetation over the area so treated, and within a very short space of time, and very little human effort. With the destruction of plants in the axils of which water constantly exists, the mosquitoes which come from these receptacles would disappear.

Just suppose we were able to successfully cope with our animal and vegetable enemies in the tropics, and that the soil were made to yield the great return of useful produce of which it is capable. Suppose that the diseases which harass and destroy

domestic animals and which undermine the health of man were eradicated. Suppose this were accomplished and mechanical energy were made available sufficient to perform all the necessary labor of agriculture, and of manufacturing processes. Would there then stand anything in the way of developing in the less hospitable parts of the warm regions of the world, a creditable civilized society? We should certainly not be despondent over the task until it has been tried.

455. **Under What Conditions Does Man Tend to Develop Best Intellectually?**—One not infrequently sees in discussions of this nature the statement that in warm regions, where food is easily obtainable, and little shelter or clothing is necessary for the comfort of man, he sinks into indolence, and remains in a state of ignorance and degeneracy. It is urged that only in such a climate as necessitates exertion and foresight during the summer in order to provide food, shelter and clothing with which to pass a severe winter in comfort, will man develop in a satisfactory way the higher virtues of civilization. The theory has been postulated that energy, aggressiveness, frugality, foresight, inventiveness, solicitude for dependents, respect for property rights and other virtues of man in his most highly advanced condition, are best fostered in a climate that offers vicissitudes, and requires that the life of the individual shall be a struggle with his environment.

Others tell us, and it appears logical, that as long as man is forced to spend his days in a struggle for existence he cannot develop his higher mental qualities. It is said that the creation of an aristocratic element in society, whose wants are supplied by the labor and sacrifice of a less fortunate group, establishes the ideal condition for fostering the mental growth that comes from reflection and the study of the ideas of others.

There is doubtless an element of truth in each of these views regarding the conditions under which man will best develop his mental capacities. Leisure is essential to certain types of creative thought. Thought is stimulated profoundly through discussion, reading and observation of the phenomena of nature. It is not yet demonstrated, however, that such creative thought is possible or probable only in temperate regions where there are frequent and pronounced changes in temperature. One of the conditions of progress is hopefulness and a realization of one's powers. In temperate regions the problems of life are less difficult to solve than they are in the tropics. The winters de-

stroy, or prevent the invasion of many forms of insect life which go unhampered in tropical climes. The cattle tick and the Tsetse-fly, which bear respectively the Texas fever and the sleeping sickness do not survive the northern winters, and the population of these regions enjoy freedom from these diseases. Cold winters limit the number of species of weeds and other noxious plants, and render the production of useful crops less laborious. These are factors of the greatest importance to agriculture and to the welfare of man. In the tropics the problems set for solution before the mind of man have been of greater magnitude and more difficult to solve. Accordingly the natives have not only not solved them, but have become crushed by them. They have suffered from lack of power to overcome their enemies, and have been forced to live the lives of fugitives in the more favored nooks where nature made conditions less disheartening. In order that he may progress, man must not be faced by insuperable difficulties. He must gain his confidence and his mastery over the forces of nature in the more favorable parts of the world. From these points of vantage, confident of his powers, he will through the work of that most valuable, although numerically very small element in the population, the laboratory investigators, acquire the necessary knowledge, then lay his plans for the conquest of one of Nature's greatest prizes, the tropics.

456. **Of All Factors Diet Is the Most Important in Determining How One Feels.**—The most fundamental of all the factors which contribute to success in any enterprise is health, and the primary factor in making a faultless organism, either human or animal, is the diet. It is not permissible to attribute the differences observed between the Bahamans and Canadians solely to climate, for their diet has been so different that there is good reason to suspect that the attitude toward work and mental effort in the two groups is in no small measure due to the way they feel. Our knowledge of the effects of an unsatisfactorily constituted diet, warrants us in attributing their characteristics to this cause. The Bahamas produce tamarinds, olives, lemons, oranges, limes, citrons, pineapples, pomegranates, figs, sapodillas, bananas, melons, yams, potatoes, cucumbers, cassiva, sugar, maize and peas as the chief edible articles. From what has been said this list of storage tissues of plants is not likely to promote health. Their bread-stuff and meats are imported from the United States. The people of Lower Canada have, on the other hand, a diet much like that of the United States, viz.: one into

which a considerable amount of dairy products enters regularly. It consists principally of cereals, legume seeds, tubers and meats, but milk, butter, cheese and cream are regular components. People will feel very differently on these two types of diet.

457. **Differences in Labor Output Observed by Huntington in North and South May Have Been in Part Due to Causes Other Than Climate.**—It is scarcely permissible to compare the work accomplished by natives of Tampa with that of workers in the northern states as Huntington has done in his studies on the effect of climate, because most of the men in Tampa are infected with hookworm, and many have or have had malaria, conditions from which the northerners are free. The southern group would also tend to live on the type of diet so common among the working classes of the South, and which has been shown to predispose to, if it does not actually cause pellagra. We should expect the southern group of workers to feel less like working than the northern one, entirely aside from climatic factors, because of the less satisfactory character of their food supply.

458. **Bad Health Conditions in the United States Notwithstanding Its Stimulating Climate.**—Let us return to the problem of the health conditions among the people of the northern United States and its causes. We are told by Terman (10) that about fourteen million of the twenty million school children in the United States are handicapped by some kind of physical defect, and that not far from two million are suffering from a grave form of malnutrition. Ten million are said to have enough defective teeth to seriously interfere with health, and as many are infected with tuberculosis, and he estimates that two million will eventually die of this disease. One million are stated to be predisposed to some serious form of nervous disorder. That the conditions are fully as bad as these figures indicate is borne out by the results of medical examination of young men for the draft in the Great War. Why this condition in our boasted favorable climate for civilization, whereas the pastoral tribes of Asia, the nomads of the desert, and the peoples of the Balkan States have no such physical handicaps? It certainly behooves us to seek to discover the cause or causes which are responsible for this condition. Climate has had its opportunity and has not saved us from our unenviable physical and health standards. As a result of my many experimental observations, I have come to hold the view that animal experi-

mentation, human geography and history, all point in an all but conclusive manner to the diet as the principal cause of our health troubles, in so far as these are not brought about by communicable diseases.

459. **Changes in the Character of the American Diet During Recent Decades.**—There have been in course of development during the last century, changes in the character of the diet of the greater portion of the inhabitants of the United States which were never suspected as of any moment from the standpoint of health until their significance was brought to light by laboratory investigations in nutrition during the last six years. Of these, probably the most important because so insidious, is the great extension of the consumption of cereal grains, and the changes in the process of preparing these for human food.

460. **The Cereal Grains as a Menace to Health.**—The results of our investigations on the nutritive value of the cereal grains disturbed a well established belief that these were highly satisfactory foods. When investigated by adequate methods they proved to be deficient in the amount and quality of their proteins, in certain mineral elements, and in two of the well demonstrated vitamins. Since all experimental results should tally with human experience it was natural that we should reflect upon the extent to which these incomplete foods enter into the human diet, and whether man has throughout long periods of his history, taken amounts comparable to what he does to-day. Any changes from long established usage in this matter should, we believed, be given careful consideration to see whether a course is being pursued which may place our health standards in jeopardy. There appears to be, in fact, a use of this class of foods to an extent which was never before practiced, and which has considerably exceeded the limit of safety.

Primitive man ate everything he could secure which was edible. His animal food included the flesh of such animals as he could catch, and also fish, eggs, birds, shell-fish, insects, etc. Among the vegetable products which he doubtless ate were fruits, berries, fleshy roots, nuts and a few other seeds of plants, among which were the seeds of those grasses which have since been developed into our cereal crops. There are relatively few regions where nuts are sufficiently abundant to furnish a regular article of diet for a sparse population during even a few months of the year. The supply of cereal grains was even more inadequate. The cereal grains are the seeds of several grasses. In a

country where no agriculture was practiced, grasses would be cropped by grazing animals and the development of seed would be greatly interfered with. As Huntington points out (8) extensive agriculture was impossible until after animals were domesticated. Such seed as was produced was borne on isolated and scattered stems and would be difficult to harvest in appreciable quantities. One exception was the wild rice plant which grew in the water and was protected to some extent from animals. It was more abundant in certain places than the seeds of any land grasses were likely to be in the unmolested fruiting condition. Rice was harvested, therefore, from very early times in parts of Asia and in some of the northern states of North America. Even in these favored regions of shallow lakes and rivers, however, rice never formed a principal component of the diet of the Indians, but only an adjutant in the fall and early winter. Grass seeds of the type of the cereal grains are always eagerly sought for at ripening by birds, and the harvest time would always be short. Maize was never a food of much importance among the Indians but served only to vary their otherwise carnivorous diet. All the higher apes eat more or less of the tender leaves which have mild flavors. After man reached the stage of development where food was regularly cooked, he was able to eat coarse vegetables of the leafy type in greater variety and in larger amounts than when he had to eat them raw, because of the difficulty of digesting some of them. Potherbs early became a regular part of the food of human beings as they advanced toward civilization. They are to-day the outstanding feature of the diet of the Chinese and Japanese.

461. Great Extension in the Cultivation of Cereals in Recent Times.—The great increase in the consumption of cereal grains in various forms as flours, cornmeal, corn grits, rolled oats and the breakfast foods with which we are familiar, is an incident in the development of modern industry, and in the change from a rural to an urban life. This has forced a great part of the population to depend upon the remainder for food, and the result has been the cultivation in ever increasing amounts of those farm crops which yield the greatest returns in the food substances which were deemed of greatest importance, viz.: energy and protein values. For many years preceding the recent discoveries regarding food values, the U. S. Department of Agriculture published numerous bulletins containing the advice to the housewife to spend a large part of every dollar invested in

food for wheat flour and other milled cereal products, and vegetable fats, because these were the purchases by which she could secure the greatest amounts of protein and energy. With each succeeding decade the acreage of the entire world which was devoted to the cultivation of cereal grains has been enormously increased for a century.

In great measure this was due to the invention of machinery which made possible the tilling of the soil and the harvesting and threshing of grain with a minimum expenditure of human labor. Furthermore, this type of agriculture in which the products of the soil and consequently its fertility were sold and transported from the farm year by year, yields the greatest profits in areas too far removed from the city to be successfully utilized for truck farming. The result has been an ever increasing consumption of cereal foods. This process was so gradual that to-day many who are fairly well versed in the principles of nutrition believe that cereals are and were from the dawn of history the most prominent and satisfactory source of human nutriment. Actually this is far from true.

462. Grass as an Enemy to Agriculture.—Huntington (8) has pointed out that the great enemy of agriculture has always been grass. Primitive man could never compete with it, and accordingly could not practice extensively the cultivation of the plants which are now our staple crops. The clam shell or the crooked stick were ineffective armament indeed for the early agriculturist. When draught animals were domesticated he became capable of eradicating grass, but then the great labor involved in harvesting and threshing cereals made their cultivation on a large scale difficult. Cereal grains were even up to comparatively recent times grown because of their keeping qualities, for in a dry state they can be preserved without deterioration for months or years. They served as a reserve food supply to be drawn upon during the less hospitable parts of the year, or as a safeguard against famine in lean years which experience showed were likely to occur. Far-sighted man doubtless adopted in some measure, throughout human history, the practice of hoarding grain as did Joseph in his management of the business of Pharaoh. During the fat years people subsisted in great measure on the products of the kine and other animals which were profitable for the herdsmen. The consumption of cereal grains to the extent of 35-45 per cent of the food supply as is now the rule in parts of Europe and America constitutes an

innovation in human experience, and there are two kinds of evidence available in abundance, which point definitely and unmistakably to the belief that we have already exceeded the limit of safety in the use of cereals, *unless careful attention is given to the choice of the remainder of the food supply.* This is necessary in order that the deficiencies of the milled grains which we use so freely may be corrected.

463. **Evidences That We Have Exceeded the Limits of Safety in the Consumption of Cereals.**—The two kinds of evidence that we are now exceeding the limits of safety in the consumption of cereal products (because of the nature of the remainder of the food supply) are: (1), the overwhelming evidence of the debilitating effects on animals of such diets as are now in common use by many families, and in some measure by European and American peoples generally, viz., the white bread, meat and potato type of diet. Other milled cereal products have, it will be remembered, essentially the same dietary properties as bolted flour; (2), the great increase in the incidence and severity of certain physical defects in man in recent times, the principal features of which are easily reproducible in animals by defective diets. We need only mention retardation of growth in children, faulty posture, tendency to nervousness and irritability, defective teeth, and faulty skeletal development. All of these and others are now clearly recognized as national health problems in the United States and other countries. It is one of the great triumphs of scientific investigation that their incidence can be most satisfactorily explained on a dietary basis. These conditions will be further considered in the concluding chapter.

464. **More About the Dietary Habits of Early Man.**—Let us return to our consideration of the dietary habits of early man. Since he was not able to cultivate cereals except on a very small scale he derived most of his sustenance from other pursuits. No one will question the statement that during the tribal stage in human history, hunting and fishing were the principal means of obtaining a livelihood. But in this stage of his development very different degrees of proficiency existed at different times, depending upon the weapons, water craft and fishing devices he knew how to construct. With no better arms than a stone or club he could not successfully hunt the larger animals. Lewis and Clark tell of a tribe of Indians that they visited during their journey to the Pacific coast in 1804-7, who were in a state of starvation while surrounded by thousands of antelope which they were not

able to kill except through running to exhaustion by men on horseback, pursuing them in relays. This condition existed even with the bow and spear in a high state of perfection.

Hunting in temperate or torrid regions offered but a very precarious means of existence for man except in a few favored regions where animals such as the bison or other stupid grazing animals of large size were abundant. The seal in the Arctic regions formed an easy prey. It was largely for this reason that very early man, whenever possible, dwelt near large bodies of water where fish and shell-fish were abundant, for they were easier to secure, and offered much greater certainty of a food supply than did hunting for large quadrupeds. A carnivorous diet derived from fish, oysters, clams, and other living creatures which the sea or the large rivers afforded, encouraged primitive man, whenever possible, to become a shore dweller. The numerous enormous shell heaps or kitchen middens, which are found along the Atlantic coast of the Americas and Europe are an illustration of this mode of life on an extensive scale on the margins of these continents. These sites of human habitations were built up through many generations of people casting aside the shells of mollusks which served them as food. Here we have an illustration of a carnivorous type of diet in which all parts of the animal were eaten. This practice was highly satisfactory from the nutritive standpoint, and very superior to the present one of eating muscle meats to the exclusion of other tissues which would make good its deficiencies.

465. Domestic Animals Made Possible the Utilization of Grass for Conversion into Human Food.—It was a great step in advance when animals from which the horse, cow, goat, sheep and camel have descended, were domesticated. With these, man was able to invade grassy plains. Their animals converted coarse herbage into milk, a human food of very excellent quality and which was never failing in its supply. Solicitude for his animals, and the problems of protecting and caring for them, stimulated mental activity and cultivated in him some of the highest attributes of human nature. But his superior nutrition assured him health and vigor, and made him capable of successfully contending with his neighbors of fertile valleys who attempted to practice agriculture, or who subsisted by hunting, and he dispossessed them, at will, of their land and property. He migrated from his home in the pasture lands only at intervals when drought threatened to destroy his flocks and herds, but when he left his home

it was always as a conqueror. The Jews, moving into Palestine; the Aryan hoards who migrated westward and peopled Europe, and the Mongols, who under Ghengis Khan and his successors dispossessed their neighboring tribes, were all pastoral peoples. Their descendants of to-day live as did their ancestors of thousands of years ago, the lives of pastoral nomads on the pasture lands of Asia, and are nourished for the most part on sour milk. The Cossacks who have for so long formed the backbone of the Russian army are from this class, and the ancestors of the Turks were, and indeed most of the rural Turkish population of to-day are pastoral in their habits, and are living examples of the fine physical development and freedom from defects, which are the inheritance of sour milk drinkers generally. The sourness of the milk which they use as food is, it should be stated, a matter of secondary importance. Prompt souring is the most effective means at their disposal for preserving milk in a wholesome condition.

466. **Changes in the Diet During the Great Industrial Era.**—The development of the modern industrial era in Europe, America, and the other parts of the world which have been colonized by Europeans, has seen gradual and progressive changes in the character of the human diet, which represent an experiment which was blindly entered into, and which is now proving a grievous failure, as attested by the pronounced tendency to physical deterioration. More and more, cereals, meats of the muscle type, and tubers have become the prominent articles which nourish the Western nations. With the great increase in population the production of dairy products has become more and more a precarious business, because of the keen competition of vegetable foods in the market. On the vast ranges of America, Australia, Argentina and elsewhere, in which there is but scanty rainfall, beef production has been economically successful and has tended greatly to discourage live stock production in regions better suited to the growing of farm crops. The dairy industry would scarcely have continued to exist until now had it not been for the discovery that the great bulk of the agricultural land of America is limited in its fertility by its low content of potassium, phosphorus, and in some places of lime, and soon becomes exhausted when cereal or other crops are grown continuously and are sold off the farms. Worn out farms exist in large numbers to-day in New England and New York and elsewhere in the East, and signs of soil depletion are evident in

parts of the great wheat-growing belt in the northwest. We have no adequate sources of potassium and phosphorus with which to replace these indispensable plant nutrients. This was recognized years ago by scientific agriculturists, and the agricultural colleges and the U. S. Department of Agriculture have urged upon farmers the necessity of maintaining a flourishing animal industry as the only means of maintaining a permanent system of agriculture. By this means the crops are fed on the farm and the fertility is in great measure preserved.

467. Iodin as a Limiting Factor in Human and Animal Nutrition in Certain Regions.—It appears to have become established by recent observations that there is danger in certain parts of the United States and elsewhere, of human beings and animals failing to secure in their food a sufficient amount of iodin. This element is present in the thyroid gland to the extent of about 0.2 per cent of the dried weight of the gland, or about 10 to 15 mgms. in the entire gland. This element is essential for the formation of an organic iodin-containing compound which acts as a hormone or regulator of metabolism. Kendall (11) has isolated this substance from the thyroid glands of animals and has given it the name thyroxin. A lack of iodin in the diet prevents the formation of this hormone and leads to hyperplasia and enlargement of the gland.

Goiter is very common around the Great Lakes, in the upper Missouri and Yellowstone valleys, in Eastern Oregon and Washington, and has been attributed to lack of iodin in the soil and water of those regions.

Salmon and trout, which are reared under hatchery conditions and fed liver and are crowded, and kept in water which is not changed frequently enough, have suffered greatly from goiter. It has been shown by Marine, Lenhart and others (12) that treatment of the water in which the fish are kept, with potassium iodid, causes retrogression of the thyroid and a return to normal. Feeding the fish upon hashed sea-fish also led to improvement in the condition of their thyroids, presumably because sea-fish contain iodin. Wild fish do not suffer from this disease. Pike and bass in Lake Erie frequently suffer from goiter (13).

In the Yellowstone river valley there has been for some time a loss of approximately one million young pigs and numerous lambs, calves and colts each year as the result of thyroid disease. This most serious problem in animal production has been studied by Smith (14), who found that it was only necessary to ad-

minister sodium or potassium iodid to the pregnant sows in order to prevent the condition. As the result of the shortage of iodin many of the pigs were born dead, others died within an hour or two while still others lived twenty-four to thirty-six hours. These pigs were born in a hairless condition, and with great enlargement of the thyroid gland.

Hart and Steenbock (15) have reported results with pigs which are confirmatory of those of Smith.

Marine and Kimball (16) studied the effects of administering sodium iodid to girls in the public schools of Akron, Ohio, on the incidence and course of goiters among them. In a complete census of the condition of the thyroid gland in the girls from the fifth to the twelfth grades of the school population in this goiterous district, it was found that 1,688 or 43.59 per cent had normal thyroids; 2,184 or 56.41 per cent had enlarged thyroids, and 594 or 13.4 per cent had well-defined, persistent thyroglossal stalks.

They administered sodium iodid to a large number of these girls, and six months later a reëxamination of their thyroids was made. The following table shows the results and also the data secured with another group of girls who did not take the prophylactic treatment.

Pupils Taking Prophylactic Treatment.	*Pupils.*	*Per Cent.*	*Pupils Not Taking Prophylactic Treatment.*	
			Pupils.	*Per Cent.*
Thyroids remained normal..........	283	100.0	637	74.0
Increased from normal to slight goiter	0	0.0	259	26.0
Small goiters (unaltered)...........	287	66.0	759	87.0
Small goiters (disappeared).........	141	33.5	10	1.2
Small goiters (increased)	2	0.5	103	11.8
Large goiters (unaltered)..........	34	66.7	106	95.5
Large goiters (decreased)..........	17	33.3	5	4.5
Total	764		1,879	
Total number of girls examined.....	4,415			

These results indicate clearly the value of the administration of suitable doses of iodids at intervals, as a means of preventing the hyperplasia of the thyroid gland.

468. **The Struggle in Agriculture Between Meat Production and Dairying.**—The struggle in the animal industry for supremacy is between meat production and dairying. Beef, pork

and mutton have the advantage in respect to palatability, for they are among our most appetizing foods. Milk cannot compete with meat in this respect. On the other hand milk is unique as a food, and especially as a supplementary food which when used in sufficient amounts corrects the deficiencies of a diet otherwise composed of cereals, tubers and meats, and is, therefore, vastly superior to meat, for the specific purpose which is of greatest significance both from the standpoint of the nation's nutrition and from the standpoint of economic agriculture. Armsby (17) has calculated from a large amount of experimental data, that because of its capacity for phenomenal growth 24 per cent of the energy of food employed in pork production may be returned by the animal as human food. The dairy cow is capable of returning at least 18 per cent of the energy of the feed she consumes, into milk, whereas the beef animal or the sheep return in the form of edible meat but 3.5 per cent of the energy of the feed which they consume. Economically, therefore, milk production is the logical business to promote, even from the standpoint of energy values in food, but since the cow utilizes for milk production a very large part of her total nutrients in the form of forage plants, either as pasturage or hay, she appears in a most favorable light as a producer of human food. Forage crops can be produced in much larger quantities on a given acreage than can cereal grains or other seed crops, so that the dairy industry is an economical method of producing human food, as well as an effective means of conserving the fertility of the soil and assuring permanency of yield in agriculture. Any industry which comes into competition with it has economic and nutritional features which condemn it in the eyes of far-seeing people.

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CHAPTER XVIII

THE MOST FUNDAMENTAL PROBLEM IN PREVENTIVE DENTISTRY

469. **Recognition of the Need of Strengthening the Social Fabric.**—Many thinking people are now calling attention to the imperative need of strengthening the social fabric. Huntington (1) points out that this can be accomplished only by improvement in the inherited factors, in the health and the training of our children. He emphasizes that good inheritance or good training can serve the individual only when health permits. It will be accepted by all that heredity and training form the most important levers of accomplishment, and that they can act effectively only from the fulcrum of health. The man or woman who is always tired, or who feels no joy in actively prosecuting the work in which he or she is engaged, who is easily disheartened and downcast because of personal prospects, who struggles on more from a sense of dread of becoming a dependent upon others than from confidence that victory will still come as a reward, is essentially the victim of poor health.

470. **The Importance of Physical Well-Being.**—The value of an individual to society will be determined in great measure by the way he feels. His capacity for energy output and activity, his estimate of himself and his attitude toward his environment, are profoundly influenced by his physical condition. That emotion cannot be separated from its physical concomitants has been for many years recognized by psychologists. Dislike of one's work, idling away of one's time, lack of enthusiasm for one's undertaking, and lack of hope, take root probably from some physical basis. Derangement of the metabolic functions is generally the underlying cause for lack of appreciation of the importance of tact, for lack of respect for others and for failure to discern the futility of antagonizing others. No elements of human conduct contribute more to bring about failure than do these.

Much unhappiness results from ease of irritation and over-

sensitiveness. One's attitude toward authority and conditions in conflict with one's desires are the results of bodily conditions. Except in relatively rare cases where mental defect is inherited there is no gloom in the mind of the physically well. There are not wanting to-day persons with wide experience, who hold the view that much of the delinquency among children and criminal tendencies among adults are due to physical defects. There is danger that we attribute too much to heredity. Treadway (1), in reporting upon his studies of delinquents, says: "Bad progenitors, pernicious environment and poor educational opportunities form an insufficient basis upon which to classify personality."

471. **Evidences of Physical Deterioration.**—Keen observers have expressed during the last century, their belief that in a large part of the population of Europe and America, physical deterioration was seriously in progress. Herbert Spencer, writing seventy-five years ago of the bodily endurance of England's people, stated that, "Thus far we have found no reason to fear trials of strength with other races. . . . But there are not wanting signs that our powers will presently be taxed to the uttermost." Twenty years ago General Sir Frederick Maurice, in discussing the health of his nation, warned England that there were grave signs of national deterioration, made evident by the failure of nearly three out of every four young men to come up to the standard required for ordinary military home service even in time of peace (2).

The lack of physical fitness was seen to lie in the universal prevalence of under-developed and feeble jaws, and inferior and decayed teeth, poorly developed nose and throat, adenoids, weak chests and indigestion. These undermine the constitution, dwarf the body and predispose to disease. The widespread prevalence of rickets in childhood, and in later life the high incidence of tuberculosis are but two of the direct manifestations of faulty development. The leading causes of this grave tendency to deterioration in the younger generation were referred to unfitness for motherhood, lack of essential knowledge on the part of parents, bottle-feeding in early infancy, defective hygiene and too much pap-feeding of children. From what has been said in earlier chapters on the basis of animal experimentation and human experience in different parts of the world, it will be evident that this explanation does not bring out with clarity, nor emphasize sufficiently the fundamental significance of the choice of food in mother and offspring.

472. **The Bottle-Feeding of Infants.**—Bottle-feeding results in serious injury to infants, principally because of ignorance regarding the kind of food necessary for their normal development. Modified milks in which wrong proportions exist among the several food elements; bad bacteriological conditions of the food or of the bottle; under-feeding or over-feeding, together with the early substitution of cereal and other foods unfit for the nutrition of infants, are the actual causes of subnormal development, rather than artificial feeding in itself. These are the causes which are undermining the vitality of the rising generation, and have already markedly reduced the stamina of the present generation of adults.

473. **Some New and Unfavorable Influences Are at Work to Undermine Health.**—If one examines the writings of those of to-day who are most active in studying the health problems of children and in arousing the nation to activity in their behalf, one finds various causes assigned for existing conditions. All would agree that we must attribute our physical deterioration to subjection of the human race to new and unfavorable conditions, but differences of opinion exist as to the nature and relative importance of these. The sedentary life; the life within houses instead of out of doors; the wearing of clothing instead of exposing the skin to the weather with its changing conditions; the eating of soft cooked food instead of raw coarse food; the debilitating effects of certain climates; the preservation of weaklings through improved hygiene and care; the artificial feeding of infants instead of nursing; the burden of responsibilities of civilized life, both mental and moral, and the failure to care for the hygiene of the mouth are among the causes most prominent. Doubtless each of these plays its part in contributing to place civilized man in many parts of the world in his present unenviable position with respect to health. It can now, however, be asserted with assurance, that the chief factor responsible for human deterioration in recent times is not included in the above list. *The chief factor lies in the unwise choice of food.*

474. **Some Observations on American School Children.**—It would be out of place here to recite at length statistics which reveal the seriousness of our own problem of malnutrition, but a few facts brought to light by the examination of a large part of the twenty million school children in the United States should be mentioned. Miss Leete, of the American Child Hygiene Association (3), summarizes these statistics by stating that ac-

cording to them 1 per cent of the children are mentally defective; that 5 per cent are tuberculous now or have been in the past; that 5 per cent have defective hearing; that 25 per cent have defective sight; that 15 to 25 per cent have diseased tonsils or adenoids; that 10 to 20 per cent have deformed feet; that 50 to 75 per cent have defective teeth and that 15 to 25 per cent suffer from malnutrition. The discovery of the nature of the defects brings forth an incentive to inquire into the causes producing them, and an understanding of the etiology of these conditions gives courage to undertake the task of rendering assistance.

475. **More Can Be Achieved Through Dietary Reform Than Through Any Other Agency.**—In preceding chapters data are presented which show the basis of the establishment of dietary habits which in great measure would bring about within two generations a return to physical standards in man closely approximating the best which have been realized in human history. There is nothing more important than the institution of dietary reforms in accordance with the scientific knowledge set forth in these pages. The validity of the conclusions drawn from human experience and animal experimentation has already been verified in several places by the scientific feeding of school children. Notable among these are the triumphs of Mrs. Ira Couch Wood of Chicago (4), and of Miss Maude A. Brown of Kansas City, Mo. (5). These results have been obtained essentially by liberal feeding of milk to undernourished school children. They represent the degree to which children who have been badly started in life and who are suffering from retardation of growth and other physical handicaps respond merely to proper feeding and rest. This tends to overcome the injurious effects of diseased tonsils, poor and infected teeth and other ailments which many have believed the clinic could successfully cope with only by means of surgery.

476. **The Story of Adam.**—Most striking among the results obtained by Mrs. Wood, of the Elizabeth McCormick Memorial Fund, is the history of Adam. This boy was in very poor physical condition, at the age of fourteen years, when the economic condition of his family required that he seek employment. He was refused a permit to work as a minor because of his frail condition. Mrs. Wood produced a complete transformation in him during twelve weeks, by feeding him liberally with milk, of which he drank large quantities. From 23 per cent under weight, he reached the normal for his height during this period, and on

again applying for a permit to work had no difficulty in passing. He was transformed from a feeble child to a strong and vigorous boy in three months by changing his diet and taking rest. Emphasis upon rest is of very great importance to children who are in a poorly nourished condition. It is impossible to appreciate the transformation of this boy, except through a comparison of his photographs before and after the dietetic treatment. There are many thousands of boys and girls in the country to-day who could be similarly transformed.

477. **Prenatal Life, Infancy and Early Childhood Are the Critical Periods.**—The greatest good is to come to the next generation, so far as educational effort can accomplish its purpose, through the solicitude of mothers and fathers in so caring for their unborn and born children as to obviate the establishment of those physical defects which not only prevent normal muscular development but which affect the entire outlook upon life. "Flat feet," or broken arches, feeble musculature and low muscle tone, which induce faulty posture, are factors determining whether the child will experience pleasure in activity and competition with his associates. One victory in a game causes a desire for other victories, and confidence in self and the belief that effort will be rewarded by achievement are the direct result of successful participation in closely contested games. Although there are many examples of great achievement by persons whose physical constitutions were below the average or even decidedly inferior, it is nevertheless true that physical handicaps usually determine the angle from which life is viewed. Children who are below the optimum in physical well-being do not radiate happiness, but tend to view the outlook with discontent and to brood over the hardness of life rather than eagerly to seek its opportunities with the expectation of bettering their own and the condition of others. Physical perfection is the greatest assurance that the individual will make an effort, and lack of effort or failure to do one's best is to the average human being the worst handicap to success.

478. **Malnutrition Is Usually the Primary Cause of Physical Inferiority in Childhood.**—Malnutrition is not, as many have hitherto believed, ordinarily the secondary result of those physical defects which the clinic seeks to remedy, but it is the primary cause from which these physical defects generally arise. Furthermore, the present widespread view that the most important task in hand is the medical treatment of those children in whom

clinically discernible defects exist is a mistaken one. First in importance both from the standpoint of the physically defective child and of the national welfare, is the establishment of nutritive conditions which are regulated as nearly as possible with the scientific precision necessary to insure optimal well-being. The clinic should occupy second place in the scheme of human betterment.

479. **The Basis of Preventive Dentistry Is Satisfactory Nutrition During Development.**—A similar error is widespread concerning the most effective method of solving the problem of protecting the teeth from decay. In a recent publication Clark and Butler (6) state "Dental caries is caused by the action of bacteria or germs, which normally inhabit the mouth. These germs, acting in the presence of food débris and certain elements in the saliva, result in the formation of an acid which attacks the enamel covering the exposed parts of the tooth, after which the underlying softer parts become rapidly destroyed. Many other factors are actual and potential causes of dental decay and its progress, such as—1. Low resistance of the teeth to decay because of developmental defect (antenatal and postnatal). 2. Faulty diet (both of the mother during pregnancy and of the child). 3. Neglect of dental attention through ignorance of the parents. 4. The cost of dental attention, a serious consideration with families of low economic status. 5. Failure of the child to call attention to the condition of the teeth, either because it is too young or because of fear. 6. Lack of dental facilities, so common in rural sections." It is pointed out by these authors that a very high percentage of undernourished children show marked evidence of dental decay. They cite the results of the examination of 270 children by the Public Health Service, which showed that 33 per cent of these had from 1 to 4 cavities, 48 per cent had from 4 to 8, and some had 9, 10 and 11 cavities. It is to be regretted that this excellent paper fails to emphasize the importance of including in the campaign for the preservation of the teeth, an effort to change the character of the nation's diet, in order that developmental defects shall grow less common and less severe as time passes. Emphasis is laid entirely upon the importance of the dental hygienists, who limit their work to cleaning and polishing all surfaces of the teeth above the gum margins, to the dental clinic for the repair of the teeth already in a state of decay and to the teaching of mouth hygiene. Such a program is based upon the belief that cleanliness of the oral

cavity is of first importance as a preventive measure for preserving the teeth. Terman (7) says: "We know that a clean tooth, a tooth that is kept clean, cannot decay." Butler (8), in a recent article states " . . . it is but a matter of a few generations before civilized man will be edentulous or without teeth. The possibility of persuading the people of to-day to subsist upon a coarser diet is most remote and it will be at once seen that our only hope in this direction lies in some prophylactic measure." He further states: "Just as in preventive medicine lies the greatest good in all medical science, so, too, in dental prophylaxis is to be found the nearest solution of this problem. The establishment of a dental clinic in a school and the employment of competent persons to care for the mouths of the younger children comes nearest to the requirements." And he further says: "Every hygienic measure adopted strengthens the position of others that may be in practice, but in the whole field of hygiene there is no single part that can approach the hygiene of the mouth in importance."

480. **The Prevailing Ideas Regarding Preventive Dentistry Are Based on Wrong Premises.**—These quotations represent fairly the position now being taken by almost if not quite all of the physicians and dentists who have, through their energy and solicitude caused the development of the present movement for preservation of the teeth of the rising generation through repair and mouth hygiene. All efforts in this direction deserve the highest commendation, but anyone who gives much thought to this subject, and who is familiar with modern research in the field of nutrition, must come to the conclusion that, valuable as is this movement for the welfare of the children of the present day, it falls lamentably short of being a comprehensive program from the standpoint of the race and the nation. But these quotations from leading authorities give a true picture of the present day situation in preventive dentistry. In England and America we are in the stage of progress where repair and cleanliness are goals toward which school authorities and parents are being urged to work. This is essentially an attractive superstructure without a firm foundation. In its present form this movement for the preservation of the nation's teeth is founded upon a plan which will call for more and ever more investment of time, money and human effort with no prospect of relief from the burden. *This is because it ignores the developmental factor.* The only logical and far-seeing policy is to inquire into the cause of the

poor quality and vulnerability of the present generation, and to take up the task of instituting reforms in our habits of living which will free the next generation from the defects from which we are now suffering.

Present activities in relation to dental prophylaxis may well be likened to the institution of a rigid quarantine in an epidemic of typhoid fever brought about by an infected milk supply, but without making any effort to check the delivery of the dangerous milk. We should not be getting at the root of the evil. *In the prevention of dental caries, the only effective measure is to adopt a policy which will result in the formation of a dental mechanism possessing its own barriers of defence.* This involves the developmental factor, which those now out of infancy no longer have the opportunity to profit by, but we can easily, if we apply the scientific principles of nutrition to the daily life of the nation, leave to our children's children the priceless heritage of freedom from the physical suffering which we ourselves must bear, not only from mouth discomfort, but from rheumatism, heart disease and other ailments having their origin in infected teeth. When dietary reforms are instituted sufficiently effective to bring about this result, and when in addition the dental clinic is established in the public schools on a scale adequate to meet the present day need for repair, we shall have a comprehensive dental program which will in due time accomplish the great objective—the eradication of dental caries. This is, however, but one of a number of most fundamental achievements to be realized by effectively carrying out such a program.

481. The Most Satisfactory Type of Diet.—In concluding this chapter it may be well to epitomize the system of living by means of which we and our descendants may recover the physical prestige we are rapidly losing owing to changed conditions of living, especially with respect to our food habits. The system of diet which can be confidently recommended with assurances that it will go a long way toward improving the physical fitness of the nation is a very simple one, and its daily practice involves no great self-denial. It involves the borrowing of the best elements in those several systems of diet which have been thoroughly tested in human experience and have been found successful.

The first and most important principle is the extension of the use of dairy products. Instead of the present consumption of half a pint of milk a day there should be at least a quart per

capita. Somewhat more than this would probably be nearer the optimum. This is the feature of the diet of all the pastoral peoples of the past and present, which made them superior in physical perfection to all other peoples. The second principle to be kept in mind is that there are dietary properties in the leafy vegetables, which are unique among foods of vegetable origin. These have been the "protective foods" for many of the Asiatic peoples. Their consumption in liberal quantities as regular constituents of the diet serves not only to provide the body with valuable nutrients it cannot secure in adequate amounts from milled cereals, tubers and muscle meats, but also serves to maintain the intestinal tract in a hygienic condition through promoting prompt elimination. Milk likewise serves, through its encouragement of the growth of lactic acid-producing organisms (which cause souring of milk), to bring about the disappearance from the intestine of those types of bacteria causing putrefactive decomposition of the food residues with the production of substances which are a physiological abomination. This principle, first enunciated by Metchnikoff, is shown by modern bacteriological studies, to be sound. Milk has, however, dietary properties which the famous bacteriologist did not discern, and which make it the one food for which there is no effective substitute.

It is essential to keep also in mind the third principle of great importance in nutrition, viz., that of taking regularly a certain amount of raw vegetable food for the specific purpose of providing the body with a sufficient amount of the anti-scorbutic substance.

If these simple principles are adhered to, the main features of an adequate diet will be fulfilled, and the remainder of the food supply may safely be derived from any of our ordinary milled cereal products, tubers, root vegetables, meats, etc. It is distinctly to be recommended on physiological grounds, however, that the consumption of meats be kept at a somewhat lower plane than is now the rule.

It would be beyond the scope of the present discussion of nutrition to discuss in an adequate way the details of putting into effect in the home the ideal system of diet. Miss Simmonds and the author have treated this subject adequately elsewhere from the point of view of the housewife (9). It must suffice here to say that aside from the liberal use of milk in the many ways in which it can enter into the diet without in any way disturbing our established food habits, the desired end is to be attained

through the daily consumption of the vegetables we class as greens or pot-herbs, and through the practice of eating salad dishes twice a day.

482. **Mistaken View Regarding the Cause of the Physical Excellence of Primitive Peoples.**—It is not essential that we retrogress to a state of social, educational or ethical inferiority in order to enjoy the physical fitness frequently seen in half savage peoples. Too much emphasis has been placed upon the beneficial effects from the standpoint of health, of hardship and exposure to which primitive man was of necessity subjected. Hardship and exposure never did anyone good. Protection from the elements is conducive to health, as is also freedom from excessive exertion. The factors which have tended to reduce civilized man to a state of physical inferiority as compared with his barbarous forebears are in great measure due to changes in the character of his diet. We can easily regulate our daily fare to be essentially optimal from the standpoint of meeting the chemical needs of the body, and at the same time to make it of a nature which will necessitate chewing for the express benefit of the development of the jaws and teeth.

483. **Concluding Statement.**—In the course of these pages, I have traced the beginnings of the development of exact knowledge of the processes of nutrition, and have shown how the science expanded through the intricate reasoning and refined experimental studies of an era, the great popularity of which has not yet begun to wane. The fundamental principles have been illustrated in all cases through the results of animal experimentation. After these fundamentals had been established there followed a study of human experience with diet, throughout history man's most pressing problem, and finally an application of the discoveries of this branch of physiological science to an interpretation of certain of the present day problems of health and their solution. It has been a joy to do this. The concentrated efforts of the author during a period of fourteen years have been devoted to observing the effects of diets of different types on experimental animals. During this time a continuous search has been carried on for information of any and every kind which would aid in correlating the results of the laboratory with those of practical experience. Year by year this has increased his conviction that the scientific discoveries in the field of nutrition are destined to be recognized as the most fundamental of the agencies that contribute to the health, happiness and achievement of man.

Some time must elapse before a full appreciation of the importance of approximating the optimum in the character of the food supply can be expected, but when appreciated at its full value, our knowledge in the field of the science of nutrition will be regarded as our most precious possession.

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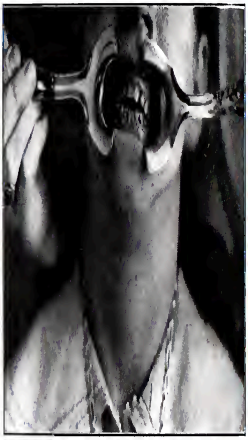

Fig. 20.—Illustrates the extent to which the teeth have degenerated among Americans in recent times. The trouble lies in great measure in faulty nutrition during prenatal life, infancy and childhood. A satisfactory diet is essential for the development of a sound set of teeth. If the jaws and teeth are poorly developed they must throughout life be vulnerable to bacterial agencies.—Courtesy of The Forsyth Dental Clinic.

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